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PSYCHOPHARMACOLOGY ABSTRACTS

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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

217686 Muller, W. E.; Wollert, U. Pharmakologisches Institut der Universitat Mainz, D-6500 Mainz, Obere Zahlbacher Strasse 67, Germany **Benzodiazepines: specific competitors for the binding of L-tryptophan to human serum albumin.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 288(1):17-27, 1975.

By means of the gel filtration technique, the effect of nine benzodiazepine derivates on the binding of L-tryptophan to human serum albumin was investigated. Using equimolar tryptophan and benzodiazepine concentrations, all benzodiazepines with binding constants higher than 10,000, displace L-tryptophan from its binding site to a high degree. The mechanism of the displacement was characterized as a competition for a common binding site. Some of the benzodiazepines displace L-tryptophan to a greater extent than salicylic acid. The benzodiazepines and tryptophan are the only substances known with a high degree of stereospecific binding to human serum albumin. This study shows that there is only one binding site on the human serum albumin molecule, which binds tryptophan and the benzodiazepines in a highly stereospecific manner. It is concluded that the benzodiazepines and L-tryptophan must have similarities in their molecular structure, so that both can bind to the common binding site in such specific manner. These considerations are discussed in regard to the known influence of benzodiazepine derivatives on the L-tryptophan metabolism in brain. 33 references. (Author abstract modified)

220951 Ammon, H. L.; Balsamo, A.; Macchia, B.; Macchia, F.; Howe, Donna-Beth; Keefe, W. E. Department of Chemistry, University of Maryland, College Park, MD 20742 **The proposal of an unified model for the interpretation of the activity of different classes of beta-adrenergic agents.** Experiential (Basel). 31(6):644-646, 1975.

A unified model for the interpretation of the activity of different classes of beta-adrenergic agents is presented, based on studies of the crystal structures of type A and B beta-adrenergic agents including propranolal, propranolol hydrochloride and dechloroisoproterenol. It is hypothesized that the O2-C4-C5 moiety in the type B beta-adrenergic drugs, as a result of the conjugation of oxygen with the haphthyl ring, can electronically and sterically simulate a protein of an aromatic ring and therefore take the place of the aryl group directly linked to the C2 atom in the type A drugs in the interaction with the receptor. This hypothesis is supported by least squares plan angle data which reveal a clear relationship between Ar-CH(OH) and Ar-O-CH2CG(OH) moieties; the angles are all in the 56 degree - 87 degree range. Small differences observed in the angles are attributed to crystal packing forces. 14 references.

221036 Borg, Jacob; Gershon, Samuel; Alpert, Murray. Neuropsychopharmacology Research Unit, New York University Medical Center, 550 Fifth Avenue, New York, NY 10016 **Dose effects of smoked marihuana on human cognitive and motor functions.** Psychopharmacologia (Berlin). 42(3):211-218, 1975.

The dose effects of delta9-tetrahydrocannabinol in humans were measured within a systematic presentation of timed cognitive and motor tests on a continuum of simple to complex functions. Graded doses of marihuana were administered to five adults in a longitudinal repeated measurements design. Speed of response was the basic parameter measured across tests of increasing cognitive involvement. Marihuana produced significant dose response effects of impaired performance in all test scores. However, single automatic motor abilities demonstrated greater sensitivity than tests of greater complexity. Evidence is presented for tolerance development. 36 references. (Author abstract)

221734 Schmutz, J. Forschungsinstitut, Wander AG, CH-3001 Berne, Switzerland **Neuroleptic piperazinyl-dibenzo-azepines: chemistry and structure-activity relationships.** Arzneimittel-Forschung (Aulendorf). 25(5):712-720, 1975.

The chemistry and the molecular and physichochemical properties of the 11-piperazinyl derivatives of dibenz(b,f)(1,4)-oxazepines and dibenz(b,f)(1,4)-thiazines and of dibenzo(b,e)(i,4)diazepines as well as those of the 6-piperazinyl-morphanthridines are reviewed. The physichochemical parameters sigma, pK, pi, RM and surface pressure are considered in relation to each other and in relation to two pharmacological effects, namely apomorphine antagonism and cateleptic activities. The influence of substituents, bridging moiety and basic side chain on structure activity are discussed. Finally, the dibenzodiazepine derivative clozapine, which differs markedly from the classical neuroleptics in its biochemical, pharmacological and clinical properties and represents a new type of antipsychotic agent, is discussed. 57 references. (Journal abstract)

221735 Tamagnone, G. F.; De Maria, R.; De Marchi, F. Research Department, Schiapparalli S.p.A., C. so Belgio, 86, I-10153, Turin, Italy **A new series of benzodiazepines: 1-hydroxyalkyl derivatives of 1,3-dihydro-2H-1,4-benzodiazepin-2-ones.** Arzneimittel-Forschung (Aulendorf). 25(5):720-722, 1975.

A series of new 1-hydroxyalkyl derivatives of 1,3-dihydro-2H-1,4-benzodiazepin-2-ones bearing a 3-hydroxyl or a 4-N oxide function together with some related compounds were synthesized and examined. One compound, 1-(2-hydroxyethyl)-3-hydroxy-7-chloro-1,3-dihydro-5-(o-fluorophenyl)- 2H-1,4-benzodiazepin-2-one has been selected for further studies in animals and in humans as an anxiety - sedative agent. 10 references. (Journal abstract)

221858 Sunjic, V.; Kuftinec, J.; Kajfez, F. Compagnia di Ricerca Chimica, Via Motta, 18, CH-6830 Chiasso, Switzerland **Chiral 1,4-benzodiazepine: VII. Cyclization rates of 2-(N-alpha-ammoniumacyl)-amino-5-chloro-benzophenones in the chiral 1,4-benzodiazepin-2-ones.** Arzneimittel-Forschung (Aulendorf). 25(3):340-343, 1975

Cyclization rates of some S-alpha-amino acid derivatives into chiral 1,4-benzodiazepin-2-ones were determined under physiologic conditions and plotted against pKA values of the corresponding alpha-amino acids. No correlation between k, i.e. t1/2 values, of the acidic precursors, and pharmacodynamic activity, as determined by some standard tests, was observed. Unambiguity of cyclization, and its t1/2 values reveal benefits in the physiochemical properties of the investigated acyclic precursors as transport forms of the chiral 1,4-benzodiazepin-2-ones with prolonged pharmacological activity. 20 references. (Journal abstract)

222633 Mosly, Soliman Ahmed. American University **Analysis of amphetamines and other psychoactive drugs: a colorimetric assay of (S)-(+)-amphetamine in the submicrogram range. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-5471 HC$13.50 MF$5.00 150 p.

A quantitative, colorimetric assay for (S)-(+)-amphetamine at the 10-100 nanogram level was developed. Reaction of (S)-(+)-amphetamine with a 10 fold or larger molar excess of 2,5-dimethoxyoxolane in glacial acetic acid - chloroform mixtures for 10 minutes (S)-(+)-1-phenyl-2-(1-pyrrolyl)-propane quantitatively. Addition of a 50 fold or larger molar excess (based on (S)-(+)-amphetamine) of (E)-p-dimethylaminocinnamaldehyde in acidic ethanol at room temperature a blue solution with long wavelength. Under appropriate conditions, the formation of the colored complex took a few minutes, while its decomposition had a halflife of 2.0hours. Blood serum or urine samples containing (S)-(+)-amphetamine were analyzed by adjustment of the pH to 8-9, extraction with an equal volume of chloroform, and treatment of the extract. Pure samples or extracts both displayed a linear dependence of the absorbance on initial concentration of (S)-(+)-amphetamine. The maximum error in reproducibility was 4% within a set of runs extracted from the same source of blood serum or urine, and 5% within sets from different blood serum or urine sources. (Journal abstract modified)

222634 Bartholow, Robert Martin. University of Iowa **Nonrigid amines and amino acids related to apomorphine. (Ph.D. dissertation).** Dissertation Abstract International. Ann Arbor, MI, Univ. M-films, No. 75-13724 HC$13.50 MF$5.00 110 p.

Three series of 1,2-diphenethylamines and one of 2,3-diphenylalanine derivatives were synthesized as part of an investigation of dopaminergic receptor(s). The three series of amines consisted of primary, secondary and tertiary amines in a 2-(3,4-dihydroxyphenyl)-1-phenethylamine series and two isomeric 2-(3,4-substituted methoxyhydroxyphenyl)-1-phenethylamine series. The amino acid series included the dihydroxy and two monomethoxy, monohydroxy primary amino acids. If the amino acids are substrates for dopa decarboxylase, certain of the amines would be produced. Possible structural rigidity activity relations of dihydrocyphenethylamines were reviewed and discussed. Conformations of the amines were examined with respect to these relationships, and the prospects for biological activity were discussed. (Journal abstract modified)

225105 Verma, Mahima; Chaturvedi, Arvind K.; Chaudhari, Anshumali; Parmar, Surendra S. Dept. of Pharmacology and Therapeutics, King George's Medical College, Lucknow University, Lucknow 226003, India **Monoamine oxidase inhibitory and anticonvulsant properties of 1,2,4-trisubstituted 5-imidazolones.** Journal of Pharmaceutical Sciences. 63(11):1740-1744, 1974.

Several 1,2,4-trisubstituted 5-imidazolones were synthesized and characterized by their sharp melting points and elemental analyses. All substituted imidazolines inhibited the activity of monoamine oxidase (MAO) in rat brain homogenate. Preincubation of the brain homogenates with the substituted imidazolones, prior to the addition of the substrate (kynuramine), did not alter the degree of enzyme inhibition. Further evaluation of one of the compounds indicated that the MAO inhibition was competitive in nature. All substituted imidazolones possessed anticonvulsant activity ranging from 20-70% at a dose of 100mg/kg; however, this activity was unrelated to their MAO inhibitory effectiveness. 17 references. (Author abstract modified)

225106 Zalipsky, Jerome J.; Patel, Dahyabhai M.; Reavey-Cantwell, N. H. Analytical and Physical Chemistry Dept., Research Division, William H. Rorer, Inc., Fort Washington, PA 19034 **Hydrolytic degradation of methaqualone.** Journal of Pharmaceutical Sciences. 63(11):1784-1786, 1974.

The degradation products from acid and base hydrolysis of methaqualone, 1-methyl-3-o-tolyl-4(3H)-quinazolinone, were isolated and identified by combined methods using liquid - liquid extraction, thin layer chromatography, gas - liquid chromatography, and infrared, ultraviolet, and visible spectroscopy. In boiling acidic or basic media, anthranilic acid, o-toluidine, and acetic acid were the major degradation components. The formation of the other degradation products, N-acetylanthranilic acid and 2-aminobenzo-o-toludide, was acid - base strength dependent. The degradation of methaqualone in basic or acidic media followed different reaction pathways, but the primary decomposition was due to hydrolytic cleavage. The relationship between the degradation product, 1-aminobenzo-o-toluidide, and 2-nitrobenzo-o-toluidide, a metabolite of methaqualone in humans, is discussed. 18 references. (Author abstract modified)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

217577 Sofia, R. D.; Harakal, J. J. Department of Pharmacology and Toxicology, Wallace Laboratories, Half Acre Road, Cranbury, NJ 08512 **Evaluation of ketamine HCl for anti-depressant activity.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 214(1):68-74, 1975.

Using several routine screening procedures to determine antidepressant drug activity in experimental laboratory animals, ketamine HCl was found to possess significant activity over a wide range of oral doses. The tests used were: 1) reversal of tetrabenazine induced ptosis in mice; 2) reversal of reserpine induced hypothermia in rats; 3) enhancement of yohimbine toxicity in mice and 4) inhibition of oxotremorine induced tremors in mice. In general, the antidepressant potency of ketamine HCL was substantially less than that of imipramine HCl. 16 references. (Author abstract)

218956 Spirtes, M. A.; Garey, Richard E. Department of Pharmacology, Tulane University School of Medicine, New Orleans, LA 70118 **Serum erythrocyte and CNS levels in rhesus monkeys of orally and intravenously administered rubidium salts.** Biological Psychiatry. 10(2):219-226, 1975.

The cerebral localization of rubidium ion after chronic ingestion of a wide concentration range of the chloride or carbonate salt and the correlation between plasma and erythrocyte levels with the quantities localized in different brain areas were studied in rhesus monkeys. The findings show that: 1) the effects of intravenous administration of rubidium ion are often toxic and unpredictable in monkeys; 2) the animals feed well and take the drug without difficulty, with no evidence of toxicity for orally ingested rubidium; and 3) rubidium ion brain levels correlate roughly with erythrocyte levels and not with serum levels. The implications of these findings for the application of rubidium in humans are considered. 10 references. (Author abstract modified)

218958 Vogel, Wolfgang H.; Lerner, Susan. Department of Pharmacology, Thomas Jefferson University, Philadelphia, PA 19107 **Methylated derivatives of norepinephrine and the conditioned avoidance response in rats.** Biological Psychiatry. 10(2):229-233, 1974.

The effects of some O-methylated and/or N-methylated norepinephrine derivatives on the conditioned avoidance response (CAR) in rats were examined. Rats were trained to criterion in a conditioned avoidance response, and their performance was assessed at various times before and after injection with norepinephrine derivatives. The injection of 100mg/kg of isonormetanephrine, isometanephrine, and N-methylistometanephrine was without effect on CAR in rats. The injection of phenylethanolamine (100mg/kg), Beta-O-methylnorepinephrine (25mg/kg), and N-methylepinephrine (100mg/kg) interfered significantly with the CAR, interference by the latter two compounds caused by a peripheral action of these chemicals. Methylated derivatives of norepinephrine are behaviorally inactive, and this lack of behavioral effects is hypothesized to be due to the presence of an hydroxyl group in the beta position of the side chain. 11 references. (Author abstract modified)

221046 York, James L.; Winter, J. C. New York State Research Institute on Alcoholism, 1021 Main St., Buffalo, NY 14203 **Assessment of tolerance to barbital by means of drug discrimination procedures.** Psychopharmacologia (Berlin). 42(3):283-287, 1975.

In order to determine the relative development of tolerance to the discriminative stimulus and hypnotic properties of barbital, rats were trained in a Skinner Box to discriminate the effect of sodium barbital injection from that of saline injection. After the rats were well trained, the administration of daily hypnotic doses of barbital for 8 days produced marked tolerance to the hypnotic effect of the barbiturate in all animals. The ability of the 80mg/kg dose to serve as a discriminative stimulus was not impaired in animals which had been trained with the drug as the condition during which bar presses had been reinforced (SD condition). Animals for which bar presses had gone unrewarded under barbital (S-delta condition) displayed a tendency to develop tolerance to the stimulus properties of barbital. These findings are interpreted in the light of dose effect studies, and it is suggested that the acquired polarity of the drug condition determined by its assignment as Sd or Sdelta0a D or S-delt may influence the discriminability of the drug in future exposures. 13 references. (Author abstract)

221268 Ferrini, R.; Miragoli, G.; Taccardi, B. Simes S.p.A., via Bellerio 41, I-20 161 Milano **Neuro-pharmacological studies on SB 5833, a new psychotherapeutic agent of the benzodiazepine class.** Arzneimittel-Forschung (Aulendorf). 24(1):2029-2032, 1974.

A new benzodiazepine derivative, 3-N,N-dimethylcarbamoyloxy-7- chlor-5-phenyl-1-methyl-1,3-dihydro-2H-1,4-benzodiazepam-2-one (SB 5833), was submitted to a number of neuropharmacological tests in mice, rats and rabbits to assess its tranquillizing properties in comparison with medazepam, temazepam, chlordiazepoxide and diazepam. The compound exhibited tranquillizing properties similar to those of medazepam. It compared favorably with medazepam regarding the ratio between toxic and active doses and the ratio between muscle relaxing and sedative effects. 9 references. (Journal abstract)

221287 Shimizu, M.; Hirooka, T.; Karasawa, T.; Masuda, Y.; Oka, M; Ito, T.; Kamei, C.; Sohji, Y.; Hori, M.; Yoshida, K.; Kaneko, H. Dainippon Pharmaceutical Co. Research Laboratories, Department of Pharmacology, 33-94, Enoki-cho, Suitashi, Osaka 564 **Pharmacological evaluation of 3-(N-3,3-diphenylpropyl-N-methyl)- aminopropan-1-ol-hydrochloride (PF-82), a new type of antidepressant drug.** Arzeneimittel-Forschung (Aulendorf). 24(2):166-173, 1974.

The pharmacological properties of 3-(N-3,3-diphenylpropyl-N-methyl)- aminopropan-1-ol-hydrochloride (PF 82) were examined in comparison with those of imipramine and other antidepressants. Actions of PF-82 closely resemble those of tricyclic antidepressants in the antagonism of reserpine syndromes in mice and rats, the blockade of muricide in rats, increased chick locomotion, potentiated yohimbine convulsion of mice, inhibited noradrenaline uptake in rat brain, potentiated noradrenaline pressor response in dogs, and absence of monoamine oxidase inhibitor activity. 30 references. (Journal abstract)

221722 Fernandez-Tome, M. P.; Fuentes, J. A.; Madronero, R.; del Rio, Joaquin. Institute of Medicinal Chemistry, National Center of Organic Chemistry, Madrid **Pharmacological properties of 6,7-tetramethylene-5-phenyl-1,2-dihydro-3H-thieno(2,3-e)(1,4 4)-diazepin-2-one (QM-6008, thiadipone), a new psychotropic drug.** Arzneimittel-Forschung (Aulendorf). 25(6):926-934, 1975.

The pharmacological actions of 6,7-tetramethylene-5-phenyl-1,2-dihydro-3H-thieno(2,3-e)(1,4)-diazepin 2-one (QM-6008, thiadipone), a new psychotropic drug, were studied in rats. QM-6008 has psychosedative effects in rodents similar to the benzodiazepines. The electroencephalographic actions in rats and rabbits of QM-6008 and chlordiazepoxide are also similar. This new compound has clear conflict attenuating properties in an approach - avoidance schedule and can be considered a potentially useful anxiolytic drug. In other operant conditioning procedures in rats, variable interval and discriminated avoidance, QM-6008 induces an increase in response rate which is not shared by chlordiazepoxide. It is concluded that this new thienodiazepine derivative can be classified as a tranquilizer of the benzodiazepine type. The sedative effects of QM-6008 are less potent and the psychostimulant effects more marked than those of chlordiazepoxide. 46 references. (Journal abstract modified)

221723 Scrollini, F.; Caliari, S.; Romano, A.; Torchio, P. Via Zambeletti, I-20021 Baranzate-Milano, Italy **Toxicological and pharmacological investigations of pinazepam (7-chloro-1-propargyl-5-phenyl-3H-1,4-benzodiazepin-2-one): a new psychotherapeutic agent.** Arzneimittel-Forschung (Aulendorf). 25(6):934-940, 1975.

The pharmacological and toxicological properties of 7-chloro-1-propargyl-5-phenyl-3H-1,4-benzodiazepin-2-one (pinazepam) were investigated and compared with those of diazepam. In mouse and rat acute toxicity, in rat motor coordination and in rat metrazol convulsion tests, pinazepam was also compared with oxazepam. Pinazepam showed a lower toxicity, hypnotic activity and muscular relaxant activity than diazepam. Pinazepam and diazepam showed similar activity in reducing aggressive behavior in mice, stimulating and exploratory behavior in rats and in potentiating hexobarbital narcosis. No clearcut differences were observed in the anticonvulsant properties of the two drugs when tested against metrazol, strychnine and electroshock induced seizures. Pinazepam differs from diazepam in its longer duration of action. The main metabolic product found in the urine of rats and dogs treated with pineazepam was oxazepam. 28 references. (Journal abstract)

221741 Asami, Y.; Otsuka, M.; Akatsu, M.; Kitagawa, S.; Inaba, S.; Yamamoto, H. Sumitomo Chemical Co., Osaka, Japan **The synthesis and pharmacology of a novel**

benzodiazepine derivative, 1-(beta-methylsulfonylethyl)-5-(o-fluorophenyl)-7ichloro-1,3 3-dihydro- 2H-1,4-benzodiazepin-2-one (ID-622). Arzneimittel-Forschung (Aulendorf). 25(4):534-539, 1975.

Some of the pharmacological properties of 1-(beta-methylsulfonylethyl)- 5-(o-fluorophenyl)-7-chloro-1,3-dihydro-2H-1,4-benzodiazepin-2-one (ID-622) were determined. As an anticonvulsant, ID-622 was more potent than diazepam and medazepam when tested with pentylenetetrazol or bemegride, but was less potent than diazepam tested with strychnine or antimaximum electroshock seizure in mice. Taming effects of ID-622 were more potent than diazepam in both electroshock induced and isolation induced fighting tests, but were less potent in both septal and olfactory bulb ablated rats tests. ID-622 had only a weak influence on spontaneous locomotor activity, and did not cause righting reflex loss. In EEG, ID-622 increased fast activity and depressed hippocampal theta waves and amygdala afterdischarge in cats. Acute toxicity of ID-622 was very low. 20 references. (Journal abstract)

221823 Ishii, Yasuo; Natsugoe, K.; Umezawa, H. Nippon Kayaku Co., Pharmaceutical Division Research Laboratories, 3-31, Shimo, Kita-ku, Tokyo 115 **pharmacological action of FD-008, a new dopamine-beta-hydroxylase inhibitor: II. Effects on central nervous system in mice and rats.** Arzneimittel: Forschung (Aulendorf). 25(2):213-215, 1975.

The effects of 5-(4'-chlorobutyl)-picolinic acid (FD-008), a new dopamine beta-hydroxylase inhibitor of fusaric acid derivatives, on the central nervous system in mice and rats were investigated. FD-008 and fusaric acid did not show marked effects on spontaneous movement, convulsion, sleeping time, tremor and conditioned avoidance response but lowered the body temperature of rats at 100mg/kg p.o. FD-008 potentiated the depressive action of ethanol on conditioned avoidance response in spite of the lack of aldehyde dehydrogenase inhibition. FD-008 markedly depressed the performance on a shuttlebox and lowered the body temperature in rats after reserpine treatment at a dose at which FD-008 per se had no effect. 14 references. (Journal abstract)

222870 Heindel, Ned D.; Schaeffer, Lee A. Center for Health Sciences, Lehigh University, Bethlehem, PA 18015 **Cyanogen condensations as a route to 3-amino-2-imino-1,3-benzothiazin-4-ones with CNS depressant potential.** Journal of Pharmaceutical Sciences. 64(8):1425-1427, 1975.

A report is presented of a new synthesis of uniquely substituted analogs of 3-amino-2-imino-1,3-benzothiazin-4-ones and their biological activities. Seven new 3-amino-2-imino-1,3-benzothiazin-4-ones, prepared from the condensation of cyanogen and 2-mercaptobenzhydrazides, were evaluated in a neuropharmacological mouse profile. Central nervous system depression was observed in several members of the class. None of the compounds was judged sufficiently active to merit more extensive studies. 10 references. (Author abstract modified)

225529 van Duijn, H.; Beckmann, M. K. F. Dept. of Neurology, Valeriuskliniek, Vrije Universiteit, Amsterdam **Dipropylacetic acid (Depakine) in experimental epilepsy in the alert cat.** Epilepsia (Amsterdam). 16(1):83-90, 1975.

The effect of dipropylacetic acid (DPA -- trademarked Depakine) on the bemegride induced convulsive threshold was investigated in alert cats. Forty five minutes after DPA 200 mg/kg was administered subcutaneously, no significant effect was obtained; 5 minutes after the same dose was administered intravenously, protection from bemegride induced seizures was pronounced. DPA did not decrease focal discharges in sensorimotor cortex produced by topical cobalt, although spread of epileptogenic activity from the focus was inhibited. DPA antiepileptic protection tested by the same procedure was about the same as that given by phenobarbital and less than that given by diazepam. It is concluded that DPA may find its major therapeutic application in treatment of absences, as clinical reports suggest. 23 references. (Author abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOG

213374 Dwivedi, Chandradhar; Harbison, Raymond D. Dept. of Pharmacology, Vanderbilt University School of Medicine, Nashville, TN 37232 **Anticonvulsant activities of delta-8 and delta-9 tetrahydrocannabinel and uridine.** Toxicology and Applied Pharmacology. 31(3):452-458, 1975.

The anticonvulsant activities of delta8-tetrahydrocannabinol (THC), delta9-THC, and uridine were studied. Findings indicate that both protect against pentylenetetrazol (PTZ) induced convulsions in mice. Neither protect against maximal electric shock induced convulsions. The anticonvulsant activities of delta8-THC and delta9-THC are not additive. ARIHUANA extract also protects against PTZ induced convulsions. The mechanism of anticonvulsant activity of delta8-THC, delta9-THC, and uridine may be similar to diphenylhydantoin, but different from phenobarbital, in that neither are effective in elevating the threshold for seizures induced by electrical stimulation. It is concluded that both compounds are unlike diphenylhydantoin because they are more effective aginst PTZ induced seizures. 14 references. (Author abstract modified)

213394 Phillips, Anthony G.; Brooke, Sheila M.; Fibiger, Hans C. Department of Psychology, University of British Columbia, Vancouver, British Columbia, Canada **Effects of amphetamine isomers and neuroleptics on self-stimulation from the nucleus accumbens and dorsal noradrenergic bundle.** Brain Research (Amsterdam). 85(1):13-22, 1975.

The possible role of noradrenergic (NA) and dopaminergic (DA) systems in intracranial self-stimulation (ICS), the rate increasing effects of D-amphetamine and L-amphetamine on ICS were determined in rats with nucleus accumbens electrodes (DA placement) or dorsal NA bundle electrodes (NA placement). The D-isomer produced a significantly greater increase in ICS than did the L-isomer in animals with dorsal NA bundle electrodes. In contrast, the amphetamine isomers were equipotent in facilitating ICS in animals with nucleus accumbens electrodes. These data suggest that there exists a correlation between equipotential effects of D-amphetamine and L-amphetamine and DA electrode placements on the one hand, and prepotent effects of D-amphetamine and NA electrode placements on the other. Pimozide and haloperidol, which in low doses are thought to specifically block DA receptors, decreased ICS obtained from both DA and NA electrode placements. It is suggested that neuroleptic drugs may produce a general disruption of operant behavior and that the decrease in ICS produced by these agents does not therefore necessarily implicate dopaminergic mechanisms in the neurochemistry of reward. 40 references. (Author abstract)

213395 Pollard, Harvey B.; Barker, Jeffery L.; Bohr, Wilhelm A.; Dowdall, Michael J. Reproduction Research Branch, NICHHD, NIH, Bethesda, MD 20014 **Chlorpromazine: specific**

inhibition of L-noradrenaline and 5-hydroxytryptamine uptake in synaptosomes from squid brain. Brain Research (Amsterdam). 85(1):23-31, 1975.

The effect of chlorpromazine (CPZ) on the specific inhibition of L-noradrenaline (NA) and 5-hydroxytryptamine (5-HT) uptake in synaptosomes from the squid brain were examined. Synaptosomes derived from squid optic lobes were found to have specific, high affinity uptake systems for a variety of neurotransmitters. CPZ inhibited the uptake of L-noradrenaline and 5-hydroxytryptamine in a competitive fashion. By contrast, CPZ did not affect uptake of choline, aspartate, glutamate or glycine. These results suggest that permeation mechanisms for both L-NA and 5-HT may have similar CPZ sensitive sites. 31 references. (Author abstract)

213398 Stone, T. W.; Bailey, E. V. Department of Physiology, University of Aberdeen, Marischal College, Aberdeen, Scotland **Responses of central neurones to amantadine: comparison with dopamine and amphetamine.** Brain Research (Amsterdam). 85(1):126-129, 1975.

The effects of amantadine directly on single cells in the cerebral cortex and caudate nucleus were examined in the rat; the responses were compared with responses to dopamine and amphetamine. Almost all the units encountered were depressed by dopamine, amantadine and amphetamine applied with outward currents of 60nA. All of these drugs could be antagonized without affecting 5-hydroxytryptamine, and it is suggested amantadine might act on central serotonergic receptors. Results rule out inhibition of reuptake as a primary mechanism of action. It is concluded that amantadine stimulated dopamine receptors either directly or via the release of dopamine from presynaptic storage sites. 16 references.

213399 Trabucchi, M.; Cheney, D. L.; Racagni, G.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **In vivo inhibition of striatal acetylcholine turnover by L-DOPA, apomorphine and (+)-amphetamine.** Brain Research (Amsterdam). 85(1):130-134, 1975.

The in vivo inhibition of striatal acetylcholine turnover in the rat brain by L-dopa, apomorphine and (+)-amphetamine is reported. All three drugs stimulated dopaminergic (DA) receptors by different mechanisms and the turnover rate of acetylcholine was decreased. The results suggest that dopaminergic neurons impinge upon cholinergic interneurons in the striatum and exert an inhibitory effect on them. The cholinergic neurons with bifurcating axons may connect in parallel to each other and also with gamma-aminobutyric acid (GABA) neurons. It is concluded that drugs which stimulate striatal dopamine receptors reduce the inhibitory influences of cholinergic neurons on the GABA neurons the rate of firing of DA neurons is reduced by the inhibitory action of the GABA neurons. 26 references.

213400 Geyer, Mark A.; Dawsey, W. John; Mandell, Arnold J. Department of Psychiatry, University of California, San Diego, La Jolla, CA 92037 **Differential effects of caffeine, D-amphetamine and methylphenidate on individual raphe cell fluorescence: a microspectrofluorimetric demonstration.** Brain Research (Amsterdam). 85(1):135-139, 1975.

In a study of the effects of caffeine, d-amphetamine and methylphenidate on individual raphe cell fluorescence, the localized changes in transmitter content of central serotonergic neurons were assessed by microspectrofluorimetric methods. The findings indicate that caffeine and amphetamine and methylphenidate have opposite effects on the intraneuronal fluorescence of raphe cell bodies. The raphe nuclei also responded differentially to a given pharmacological treatment. One hour after caffeine, fluorescence was increased in both the dorsal and median raphe. After treatment with amphetamine or methylphenidate, no significant effect on the fluorescence intensity of median raphe neurons was observed. However, the dorsal raphe cells bodies exhibited marked reductions on fluorescence. 13 references.

213401 Gerson, Sylvia; Baldessarini, Ross J. Psychiatric Research Laboratory, Massachusetts General Hospital, Boston, MA 02114 **Selective destruction of serotonin terminals in rat forebrain by high doses of 5,7-dihydroxytryptamine.** Brain Research (Amsterdam). 85(1):140-145, 1975.

Selective destruction of serotonin (5-HT) terminals in rat forebrain by high doses of 5,7-dihydroxytryptamine (DHT) is reported. DHT used in combination with desmethyimipramine (DMI) to protect norepinephrine (NE) neurons produced a marked depletion of serotonin in the forebrain as well as a large decrease in the high affinity uptake of serotonin by synaptosomes prepared from this region. The drug combination was selective for its effect on 5-HT neurons as the level of NE and the uptake of low concentrations of NE, dopamine, choline, gamma-aminobutyric acid, glutamic acid and glycine were not significantly affected. The actions of DMI on NE containing nerve terminals are not restricted to blocking uptake of NE itself. 19 references.

213430 Urban, I.; De Wied, D. Rudolf Magnus Institute for Pharmacology, Medical Faculty, University of Utrecht, Utrecht, The Netherlands **The influence of ACTH4-10 on hippocampal and thalamic synchronised activity in rats.** Brain Research (Amsterdam). 85(1):195-196, 1975.

At the 6th annual meetings of the European Brain and Behaviour Society, a study of the influence of ACTH4-10 on hippocampal and thalamic synchronized activity in rats was presented. Electrical stimulation in the medial part of the reticular formation induces theta activity in the hippocampus and posterior thalamus. This response is quite stable and reporducible within and among the sessions. Power spectra of induced activity have been taken as a parameter to measure peptide effects. Averaged power spectra from placebo treated sessions were compared with averaged power spectra from sessions under peptide influence. Subcutaneous administration of ACTH4-10 produced a 0.5Hz shift in dominant frequency and an increase in the amplitude of higher frequencies in the theta band. This pattern of synchronised activity was found in the hippocampus as well as in the posterior thalamic region. Similar changes in power spectra could be mimicked by a slight increase in stimulus intensity. The effect was maximal between 60 and 120 min and lasted at least 6 h. These results suggest that ACTH4-10 facilitates transmission in midbrain limbic circuits. (Journal abstract modified)

213433 Sahakian, Barbara J.; Iversen, Susan D. Department of Psychology, University of Cambridge, Cambridge CB2 3EB, England **The effects of psychomotor stimulation on stereotypy and locomotor activity in socially deprived and control rats.** Brain Research (Amsterdam). 85(1):197, 1975.

At the 6th annual meeting of the European Brain and Behaviour Society, a study of the effects of psychomotor stimulation on stereotypy and locomotor activity in socially deprived and control rats was presented. Using measures of locomotor activity and stereotypy, dose response curves to several psychomotor stimulant drugs were obtained on rats

reared in deprived or normal environments. After both 0.5mg/kg and 1.5mg/kg D-amphetamine, the deprived rats exhibited more intense stereotyped behavior than control rats; at 5.0mg/kg, both groups showed maximum response. However, there were no significant differences between the two groups in locomotor response. A similar pattern of results was found for pipradrol, cocaine, and apomorphine. The findings show that different social and environmental experience can modify the response to dopaminergic stimulating agents. The results also suggest that stereotyped behavior should not be considered on the same continuum as locomotor activity. These two behaviors may be mediated by different mechanisms. (Journal abstract)

213450 Dankova, Jana; Boucher, Rene; Poirier, Louis J. Laboratories De Neurobiologie, Faculte De Medecine, Universite Laval, Quebec, Canada G1K 7P4 **Role of the striopallidal system and motor cortex in induced circus movements in rats and cats.** Experimental Neurology 47(1):135-149, 1975.

The role of the striopallidal system and motor cortex in induced circus movements in rats and cats was examined. Rats with a unilateral lesion of the pallidum and neostriatum or of the entopeduncular nucleus transiently display slow circus movements towards the side of the lesion. The administration of L-DOPA with a peripheral decarboxylase inhibitor (RO4-4602) or of piribedil (ET 495) resulted in similar circus movements in both groups. The injection of apomorphine or d-amphetamine is also associated with ipsiversive circling which, however, is more rapid in rats with an entopeduncular lesion than in rats with a striopallidal lesion. Chlorpromazine and haloperidol cause both groups of rats to turn slowly and towards the unoperated side. Cats with a unilateral lesion of the entopeduncular nucleus also display circus movement towards the side of the lesion during several days postoperatively. This behavior (ipsiversive circling) is slightly exaggerated by ET 495 and markedly increased by L-DOPA (administered withoug a peripheral decarboxylase inhibitor), apomorphine and d-amphetamine. 28 references. (Author abstract modified)

213474 Faeder, I. R.; Matthews, J. A.; Salpeter, M. M. Department of Anatomy, Duke University Medical College, Durham, NC **(3H)Glutamate uptake at insect neuromuscular junctions: effect of chlorpromazine.** Brain Research (Amsterdam). 80(1):53-70, 1974.

The effect of chlorpromazine on glutamate uptake was examined at the insect neuromuscular junction. Chlorpromazine, which is known to interfere with transmitter reuptake in a variety of systems, was added to the (3H)glutamate incubation medium after prolonged nerve stimulation. It was found that chlorpromazine decreased the stimulation enhanced uptake to a varying extent in the different muscle and sheath compartments. It did not affect uptake by tracheole cells and had its major effect at the neuromuscular junctions. Chlorpromazine decreased the junctional sheath uptake to the level of the nonjunctional sheath, thus eliminating the differential sheath uptake. In the muscle, chlorpromazine did not completely eliminate the difference between junctional and nonjunctional uptake, but decreased it greatly. The data suggest that the various pools depleted by nerve stimulation are replenished by different uptake mechanisms. The finding that chlorpromazine has its major effect on the uptake into junctional compartments is consistent with the hypothesis that the junctional sheath and postsynaptic muscle regions are sites of transmitter inactivation by reuptake. 66 references.

213478 Litteria, M.; Thorner, M. W. Neurology Service, VA Hospital, Downey, IL 60064 **Inhibitory effect of neonatal estrogenization on the incorporation of (3H)lysine in the Purkinje cells of the adult male and female rat.** Brain Research (Amsterdam). 80(1):152-154, 1974.

In an autoradiographic study to determine if neonatally administered estradiol influences the incorporation of (3H)lysine into proteins of the three layers of the adult cerebellar cortex, rats were injected with 17-beta-estradiol benzoate (EB). Incorporation of lysine into proteins of the Purkinje cells of adult male and female rats injected with EB was significantly reduced below control levels. Neonatally administered EB was without effect on the incorporation of lysine into proteins of the granule cells and stellate cells of the molecular layers. Incorporation of lysine into the Purkinje cells of the control and EB treated males was greater than that for control and EB treated females. Results indicate that both the sex steroids are capable of inducing long-term postnatal effects on a brain structure not traditionally associated with reproductive and sexual activity. 17 references.

213479 Sze, Paul Y.; Yanai, Joseph; Ginsburg, Benson E. Department of Biobehavioral Sciences, University of Connecticut, Storrs, CT 06268 **Adrenal glucocorticoids as a required factor in the development of ethanol withdrawal seizures in mice.** Brain Research (Amsterdam). 80(1):155-159, 1974.

Data demonstrating that a similar requirement for adrenal glucocorticoids exists in the development of sound induced withdrawal seizures in mice receiving chronic ethanol treatment are presented. The effect of adrenalectomy in reducing the incidence of withdrawal seizures was reversed by corticosterone replacement, demonstrating a glucocorticoid dependent mechanism in the chronic action of ethanol in inducing withdrawal seizures. Treatment with corticosterone alone did not potentiate the occurrence of audiogenic seizures in mice when ethanol was not administered. It is concluded that the hormone itself was not a causal factor in the induction of the seizures. 19 references.

213480 Yamamura, Henry I.; Kuhar, Michael J.; Snyder, Solomon H. Department of Pharmacology and Experimental Therapeutics, Baltimore, MD 21205 **In vivo identification of muscarinic cholinergic receptor binding in rat brain.** Brain Research (Amsterdam). 80(1):170-176, 1974.

Muscarinic cholinergic receptor binding was identified in vivo in order to evaluate the feasibility of light autoradiographic localization of 3-quinuclidinyl benzilate (QNB) and to evaluate alternations in receptor binding after pharmacological and physiological manipulations. Several lines of evidence indicated that (3H)QNB accumulation in the brain predominantly involve muscarinic cholinergic receptor sites. The relative amounts of QNB binding in the brain regions examined paralleled their relative number of muscarinic cholinergic receptor sites determined by in vitro (3H) QNB binding studies. QNB accumulation could be prevented by relatively low doses of atropine but not by a nicotinic cholinergic antagonist or noncholinergic drugs. The maximal number of binding sites for the QNB in the corpus striatum and hippocampus appears to be within an order of magnitude of the number of sites calculated from in vitro studies. 21 references.

213481 Olesen, O. Vendelin; Jensen, Jorgen; Thomsen, Klaus. Psychopharmacology Research Unit, Aarhus University Institute of Psychiatry, DK-8240 Risskov, Denmark **Effect of lithium on glucagon-stimulated cyclic AMP excretion in rats.** Acta Pharmacologica et Toxicologica (Copenhagen). 35(5):403-411, 1974.

The effect of lithium on gluagon stimulated cyclic adenosine monophosphate (AMP) was examined in rat excretion. Rats were given food containing lithium in amounts leading to serum lithium concentrations of 0.6-1.1mM, and the urinary excretion of cyclic AMP after subcutaneous injection of glucagon was determined. The unstimulated cyclic AMP excretion was the same in the lithium treated and in the control rats, but after glucagon administration the lithium treated rats excreted significantly higher amounts of cyclic AMP than the control rats. This occurred whether lithium had been given during 2 days or 6 weeks before the glucagon injection. At all dose levels of glucagon, the response of the lithium treated rats was about 70% higher than in the control rats. The increased cyclic AMP excretion was not due to the lithium induced polyuria since the difference between the lithium treated rats and control rats was also present when polyuric lithium rats were compared with polyuric control rats. 14 references. (Author abstract modified)

213482 Jensen, Jorgen. Psyphopharmacology Research Unit, Aarhus University Institute of Psychiatry, DK-8240 Risskov, Denmark **The effect of prolonged lithium ingestion on morphine actions in the rat.** Acta Pharmacologica et Toxicologica (Cophenhagen). 35(5):395-402, 1974.

The effect of prolonged lithium ingestion on morphine action was examined in rats. Ss were given lithium with the food in a dose which maintained the serum lithium concentration at about 1.0mM. Morphine, given subcutaneously in a dose of 8mg/kg body weight, was administered both acutely and chronically. Lithium increased the analgesic effect of morphine but did not affect tolerance development. Following chronic morphine administration, lithium increased the hyperthermic action of morphine and the morphine-induced motor hyperactivity. The interaction of lithium with morphine may take place through brain amines and brain cyclic adenosine monophosphate. 18 references. (Author abstract)

213483 Kierkegaard-Hansen, Axel. Psychopharmacology Research Unit, Aarhus University Psychiatric Institute, DK-8240 Risskov, Denmark **The effect of lithium on blood pressure and on plasma renin substrate and renin in rats.** Acta Pharmacologica et Toxicologica (Copenhagen). 35(5):370-378, 1974.

The effect of lithium on blood pressure and plasma renin substrate and renin was examined in the rat. For 2 months, two groups of rats were given food containing 0 and 40mmol lithium/kg dry weight, respectively. Most of the lithium treated rats gained weight, although at a lower rate than the control rats. They showed no significant changes in intra arterial blood pressure (determined in sodium amytal anaesthesia), plasma renin substrate, or plasma renin. A few lithium treated rats lost weight and developed severe lithium intoxication. Their blood pressure was also unchanged, but they showed a fall to zero in plasma renin substrate concentration. The results do not support previous observations of a lithium induced blood pressure increase. They indicate that animals with severe lithium intoxication resemble adrenalectomized animals given an insufficient supply of sodium. 18 references. (Author abstract modified)

213589 Moyersoons, F.; Giurgea, C. E. Department of Pharmacology, UCB Pharmacuetical Division, Brussels, Belgium **Protective effect of piracetam in experimental barbiturate intoxication: EEG and behavioural studies.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 210(1):38-48, 1974.

The protective effect of piracetam in experimental barbiturate intoxication was examined in rabbits. Piracetam was found to protect rabbits against the consequences of an overdose of barbiturates. When given intravenously, or by oral route, 1 hr before a dose of secobarbital which killed most of the control animals, piracetam significantly protected against death and toxic EEG signs. Posttreatment by piracetam against allobarbital intoxication was also very effective. The correlation existing between these pharmacological studies and preliminary clinical observations and also about the interpretation of the antitoxic activity of piracetam in the given experimental conditions, is discussed. 16 references. (Author abstract)

213591 De Angelis, L.; Soranzio, M. R.; Traversa, U.; Vertua, R. Institute of Pharmacology, University of Trieste, 34100 Trieste, Italy **5-Hydroxytryptamine-14C and dexamphetamine-14C uptake by fundal sarcolemma preparations and the problem of the common receptor.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 210(1):99-107, 1974.

A method of isolating the smooth muscle membranes from rat gastric fundus is described and the ability of this preparation of binding 5-hydroxytryptamine-14C and dexamphetamine-14C, as an indirect approach to the problem of the receptor for both drugs, was evaluated. The uptake of the two drugs is measured in normal preparations and after blocking the serotonin receptor with methysergide. Electron microsocpe control shows that the preparations obtained ensure a good grade of purity, since the main constituent is represented by sarcolemmic membranes. The results indicate that the membrane preparations give a clear and more specific picture of the bidning of 5-hydroxytryptamine and dexamphetamine than the tissue in toto, previously examined. Kinetic studies performed to assess the pattern of inhibition in the binding of serotonin and dexamphetamine by methysergide, indicate that both drugs bind to membrane preparations and to the receptor in a very similar manner. This suggest and at least partially supports, the hypothesis of a common receptor for both drugs. 15 references. (Author abstract)

213601 Baker, Walter W. Philadelphia College of Pharmacy and Science, Philadelphia, PA 19104 **Neuropharmacologic studies of local brain function.** Psychopharmacology Bulletin. 11(2):39-40, 1975.

The role played by neurotransmitters in governing the normal and abnormal functioning of the central nervous system is being studied in cats. The influence of psychoactive drugs on natural substances which regulate the caudate, hippocampus, and other key areas of the brain is being investigated. Intracaudate d-amphetamine produces tremors at both small and moderate dosage levels, while much higher doses of pharmacologically related methylphenidate are not tremorgenic. These results indicate the presence of qualitative differences and synergistic interaction between the two stimulants on local caudate mechanisms.

213602 Berl, Soll. Columbia University, New York, NY 10027 **Drugs, catecholamines and Krebs cycle interaction (CNS).** Psychopharmacology Bulletin. 11(2):40, 1975.

The effects of catecholamines on the turnover rates of certain amino acids (glutamic acid, glutamine, aspartic acid, and gamma-aminobutyric acid) and on compounds which play a part in the Krebs cycle, a metabolic cycle through which energy is produced from glucose or an acetyl equivalent, are being studied in rats. The way various psychotropic drugs affect the body's use of catecholamines is being defined. Intracisternal

administration of 6-hydroxydopamine resulted in marked changes in metabolism of glutamate and associated amino acids.

213603 Breese, George R. University of North Carolina, Chapel Hill, NC 27514 **Biochemical pharmacology of brain amine mechanisms.** Psychopharmacology Bulletin. 11(2):40-41, 1975.

Central biogenic amine mechanisms in relation to brain function are being studied. Research consists of a series of projects on the pharmacology of centrally acting drugs, control of behavior, development of the central nervous system (CNS) and the function of hormones in the CNS. Experiments indicate that shuttlebox avoidance responding and bar-pressing performance are dependent upon intact dopaminergic systems. A dopaminergic system other than that of the caudate is responsible for the acute aphagia and adipsia that accompanies the interruption of dopaminergic fibers in the brain.

213604 Coward, James K. Yale University School of Medicine, New Haven, CT 06520 **A mechanistic study of biological transmethylation.** Psychopharmacology Bulletin. 11(2):41, 1975.

The process of methyl transfer from the ubiquitous methyl donor, S-adenosylmethionine, to various acceptor molecules is being studied. The objective is to design drugs which will block specific transmethylations. A number of structural analogs of S-adenosylhomocystein have been synthesized and their interaction with catechol-O-methyltransferase and other methylases has been investigated. Results are in accord with the concept of a mechanism for random binding of substrates and products to the enzyme.

213605 Fox, Kevin A. State University College, Fredonia, NY 14063 **Benzodiazepines, reproduction, and development.** Psychopharmacology Bulletin. 11(2):41-42, 1975.

The effects of certain benzodiazepine tranquilizers on reproduction, development, and spontaneous behavior of mice, including olfactory dependent social and sexual activity, are being studied. All drug treatments prolong and/or inhibit estrous cycles. Mating behavior is significantly affected by the drug treatments. A delay in sexual maturation is seen in all males and females born to treated parents.

213606 Freedman, Daniel X. Department of Psychiatry, University of Chicago, Chicago, IL 60637 **LSD, psychotogenic procedures, and brain neurohumors.** Psychopharmacology Bulletin. 11(2):42-43, 1975.

The neurochemical and behavioral effects of hallucinogenic drugs, principally LSD, on brain neurohumors are being studied in several species. Research is directed toward understanding the mechanism of action of these drugs, the nature of their interaction with mechanisms which govern the brain amines, and the role of the brain amines in neurobehavioral function. Drug pretreatments and midbrain or hypothalamic lesions as well as raphe stimulation are used to probe experimentally the interactions between LSD and serotonin (5-HT) and between amine activity and behavior. The LSD induced increase in brain 5-HT in vivo has been localized subcellularly in the synaptic vesicle fraction. In vitro studies in brain slices and subcellular particulates indicate that 5-HT uptake by synaptosomes shows a substrate dependence which suggests high affinity as well as low affinity uptake systems. Studies of stereospecific binding of LSD in rat brain synaptosomal suspensions indicate that binding, like 5-HT uptake, is temperature dependent. The effect of LSD on brain 5-HT is contingent upon the availability of intact synaptic vesicles, which are the binding site of LSD induced 5-HT increases.

213607 Gibb, James W. University of Utah, Salt Lake City, UT 84112 **The role of tyrosine transaminase in brain function.** Psychopharmacology Bulletin. 11(2):44, 1975.

The activity of brain tyrosine transaminase and the effect of amphetamines on brain and adrenal tyrosine hydroxylase are being investigated, using standard biochemical techniques in the analysis of rat and sheep brains. Tyrosine transaminase activity in the brain has been found primarily in the mitochondrial fraction with some activity accessing in the nuclear fraction; transamination is the major metabolic pathway of tyrosine in both brain and liver. Repeated doses of methamphetamine significantly increase adrenal tyrosine hydroxylase activity in rats, while enzyme activity in the corpus striatum decreases. Striatal dopamine levels follow the decrease in enzyme activity and fail to increase as the enzyme recovers, while striatal norepinephrine levels remain essentially unchanged by methamphetamine.

213608 Green, Jack P. Mount Sinai School of Medicine, New York, NY **Psychopharmacologic activity: quantum chemical study.** Psychopharmacology Bulletin. 11(2):44-45, 1975.

Research directed toward the correlation of biological activities of psychotropic compounds with their structural features to show how neural tissue interacts with these drugs is reported, and the pharmacological effects of substances which have related chemical structures are predicted. The physical properties of the compounds are determined through a combination of mathematical analysis (based on quantum mechanics) and physiochemical measurement. In the pharmacological studies, observational and quantitative analyses of drug action are made in isolated enzyme systems, isolated tissue, and intact rats. The structure of various indoles is correlated with their neural and behavioral effects. The potencies of various hallucinogens can be correlated with their molecular orbital characteristics and chemical structures. In some compounds, specific types of biological activity can be predicted on the basis of chemical structure and electron configuration.

213609 Greengard, Paul. Yale University, New Haven, CT 06520 **Antipsychotic drugs: roles of cyclic AMP.** Psychopharmacology Bulletin. 11(2):45, 1975.

The effect of neural activity on the levels of cyclic adenosine monophosphate (CAMP) in various tissue preparations is being studied. Preliminary results support the hypothetical role for CAMP in the physiology of synaptic transmission in sympathetic ganglia. A mechanism by which CAMP might mediate dopaminergic transmission in the ganglion and thereby modulate nicotinic cholinergic transmission through the ganglion is outlined. This modulation is of an inhibitory type, producing a negative feedback and limiting the effectiveness of subsequent impulses in the presynaptic excitatory fibers.

213610 Hartmann, Ernest L. Massachusetts Mental Health Research Corp., Boston, MA **Pharmacological studies of sleep.** Psychopharmacology Bulletin. 11(2):45-46, 1975.

The acute and chronic effects of various psychotropic drugs and naturally occurring active compounds on sleep are being studied. In polygraphic studies using human subjects, the effects of reserpine, amitriptyline, chlorpromazine, chlordiazepoxide, and chloral hydrate are analyzed in terms of al-

terations in sleep cycling and are correlated with personality typology measured on psychometric scales. Other studies with human and animal subjects are designed to assess the impact of glycine, leucine, l-tryptophan, and other biochemicals on sleep cycling.

213611 Harvey, John A. University of Iowa, Iowa City, IA 52240 **Effect of central nervous system lesions on drug action.** Psychopharmacology Bulletin. 11(2):46-47, 1975.

The relationship between the anatomy of the brain and the chemical systems involved in motivation, learning, and sleep is being studied in rats. The anatomical systems of the brain which regulate neurochemical processes, the relationship between changes in brain chemistry and changes in behavior or sensitivity to drugs in lesioned animals, and the degree to which functional effects of brain damage can be reversed by chemical means are also being explored. Preliminary results indicate that morphine effects may involve a direct action on dopamine receptors in the caudate nucleus.

213613 Heller, Alfred. University of Chicago, Chicago, IL 60637 **Limbic system lesions and brain neurohumors.** Psychopharmacology Bulletin. 11(2):48, 1975.

The effects of central nervous system lesions on monoamines and other pharmacologically active substances and their biosynthetic enzymes in the brain are being studied in rats. Specific areas of investigation include the comparative effects of lesions in the brains of developing and mature animals, the role of peripheral and central fibers in biosynthetic processes of the pineal gland, and the transsynaptic effects of the tissue destruction. Unilateral lesions transecting the medial forebrain bundle and medial aspect of the internal capsule resulted in unilateral reduction of telencephalic monoamines and an increase in glycogen in the caudate nucleus ipsilateral to the lesions. These findings, combined with results of an analogous experiment with 6-hydroxydomanine, indicate that the mechanism by which loss of amines occurs is critical to the resulting metabolic events. Results of lesions of the nigrostriatal pathway in neonates indicate that the integrity of the nigrostriatal pathway is essential both for maintenance and development of normal carbohydrate metabolism in the neostriatum. In other experiments, electrical and chemical manipulations utilized in an attempt to reverse neurochemical deficits in biosynthesis caused by brain damage have been ineffective in reinstating lesion induced reductions in enzyme and monoamine processes.

213616 Levine, Ruth R. Boston University School of Medicine, Boston, MA **Physiologic factors in psychotropic drug therapy.** Psychopharmacology Bulletin. 11(2):50, 1975.

The effect of the normal physiological functions of the gastrointestinal tract on drug absorption by the body is being studied in rats. The influences that variations in intestinal conditions and functions can have on assimilation of psychotropic drugs, particularly those used in the treatment of mental illness, are being explored. A method for assaying chlorpromazine (CPZ) in intestinal tissue has been developed that yields complete recovery of CPZ unaltered by the conditions of determination. Preliminary experimental results suggest that no adjustment of drug dosage is required for agents such as chronically used CPZ and diphenylhydantoin upon coadministration with antibiotics to humans.

213617 Maickel, Roger P. Indiana University Foundation, Indianapolis, IN **Disposition and action of drugs affecting behavior.** Psychopharmacology Bulletin. 11(2):51, 1975.

New analytical methods for the assay of psychoactive drugs and their metabolites in biological preparations are being developed and the physiological disposition of these compounds is being studied. Comparative investigations of drug metabolism in differennt species of animals are being conducted, correlating behavioral effects of psychotropoic agents with plasma and tissue levels.

213618 Margolis, Richard U. New York University Medical Center, New York, NY **Studies on mucopolysaccharides in brain.** Psychopharmacology Bulletin. 11(5):51-52, 1975.

Biochemical and pharmacological studies are made of the role of mucopolysaccharides in neural processes. The involvement of these substances in axonal transmission of nerve impulses through effects on ion movements, binding and storage of neurohumor amines, or regulation of catecholamine biosynthesis is being explored. Mucopolysaccharides seem to be present as an extracellular ground substance or cell surfac coating in the central nervous system; they may play a role in the formation of specialized types of cell contacts, such as synaptic junctions, by mediating specific cell - cell interactions.

213620 Moore, Kenneth E. Michigan State University, East Lansing, MI 48823 **Catecholamines as central nervous transmitters.** Psychopharmacology Bulletin. 11(2):53, 1975.

The role of norepinephrine (NE) and dopamine as central nervous system transmitters is being studied. An attempt is made to effect their release from areas near the ventricular system in the brain. Amphetamine, amantadine, and tyramine have been found to selectively release H3-dopamine from the caudate nucleus into the perfusing cerebrospinal fluid; relase can be increased by electrically stimulating various sections of the nigrostriatal pathway, including terminals in the caudate, axons in the diencephalon, and cell bodies in the substantia nigra. In related studies, it has been found that NE is synthesized in neuronal cell bodies in the superior cervical ganglion at a rapid rate independent of neuronal activity, while synthesis in the terminals of these axons proceeds at a comparatively slow rate. As stimulation increases NE synthesis in terminals but not in cell bodies, it is concluded that NE concentrations in the two parts of the neuron are regulated by independent mechanisms.

213621 Morgane, P. J. Worcester Foundation for Experimental Biology, Shrewsbury, MA **Neurophysiological role of serotonin.** Psychopharmacology Bulletin. 11(2):53-54, 1975.

The neurological bases of responses to drugs which produce psychological and emotional changes in humans are being studied in rats and cats, including brain mechanisms involved in the action of serotonin. Stimulation of the locus coeruleus inhibits the activity of the anterior raphe serotonergic units, suggesting that one effect of activation of the locus coeruleus may be to decrease serotonin release in the terminals of anterior raphe projections. LSD inhibits firing of anterior raphe cells; this inhibition is of the same general extent as that seen following electrical stimulation of the locus coeruleus. In other experiments, the effects of various pharmacological manipulations in sleep are being investigated. Emphasis in these studies is on determining the effect of chemical and electrolytic lesions in specific amine coded chemical pathways on the subsequent action of psychopharmacological agents.

213624 Piette, Lawrence H. University of Hawaii, Honolulu, HI 96822 **Free radicals in psychotropic drug action.** Psychopharmacology Bulletin. 11(2):56, 1975.

The possibility that psychotropic drugs might produce their effects by altering membrane permeability is being investigated, using rats, mice, and cells from several kinds of animals. It has been found that the protein structure of red blood cell membranes can be changed in vitro by drugs such as chlorpromazine, perphenazine promazine, 7-hydroxychlorpromazine, desipramine, and imipramine; no effect is produced by phenothiazines. Similar drug effects are observed in nerve ending membranes but at much lower concentrations. Probe implantation technology is being developed in order to monitor psychotropic drug transport and facilitate detection of the drug free radical in vivo.

213625 Robins, Eli. Washington University School of Medicine, St. Louis, MO **Behavioral neuroendocrinology: chemical correlates.** Psychopharmacology Bulletin. 11(2):56-57, 1975.

The chemical correlates in the brain of various behavioral changes mediated by neuroendocrinological alterations are being studied in rats, using quantitative histochemical techniques supplemented by immunochemical methods. The metabolic events occurring in the hypothalamus during sexual development and behavior are being examined, along with estrus, castration, and androgen sterilization; thermoregulation, hunger, and thirst; and thyrotropin, adrenocorticotropin, and somatotropin regulation. Chemical analyses are made of specific nuclei of the hypothalamus controlling these behavioral - physiological interactions and of the extrahypothalamic structures modulating these interactions. Analyses of malic dehydrogenase, lactic dehydrogenase, glutaminc dehydrogenase, and glucose-6-phosphate dehydrogenase in 16 regions of the hypothalamus, cortex, cerebellum, and liver in normal adult male rats have been completed. Distribution of enzyme within the hypothalamus is found to be markedly heterogenous.

213626 Roth, Robert H. Yale University, New Haven, CT 06520 **Gamma-hydroxybutyrate and control of dopaminergic neurons.** Psychopharmacology Bulletin. 11(2):57-58, 1975.

The normal amounts of gamma-hydroxybutyrate (GHB) in the mammalian brain, the processes underlying GHB metabolism, and the interaction of GHB with dopamine containing neurons in the central nervous system are being studied. The possible role of GHB in inducing and maintaining sleep and in causing various sleep disorders is being explored. Findings suggest that the increase in dopamine caused by both GHB and electrothermic lesioning of the dopamine pathway resulted from an inhibition of impulse flow in the nigrostriatal pathway.

213627 Sabelli, Hector C. Chicago Medical School, Chicago, IL **Pharmacology of neural modulation and transmission.** Psychopharmacology Bulletin. 11(2):58, 1975.

The biochemistry and physiology of the central nervous system (CNS) are being studied in several species, along with the pharmacology of a series of compounds related to the classical biogenic amines. It is hypothesized that these substances, including endogenously formed precursors, metabolites, and byproducts of the metabolism of catecholamines and serotonin, may play a modulator role in monoaminergic synapses. These compounds are being tested for ability to produce changes in subject's electroencephalograms, behavior (activity, sleep, exploration, and hostility), visual functions as measured by evoked potentials, and the electrical activity of cortical neurons. Results show that the neurohormone, 2-phenylethylamine (PEA), is present in many brain areas, is formed from phenylalanine, and metabolized to phenylethanolamine, tyramine, and phenylacetic acid. PEA excretion is reduced in depressed patients, but this symptom is not pathognomonic of affective disorders.

213629 Schlesinger, Kurt. University of Colorado, Boulder, CO 80302 **The psychopharmacology of audiogenic seizure.** Psychopharmacology Bulletin. 11(2):59, 1975.

The biochemical and genetic causes of seizures are being studied, with emphasis on the possible role of gamma-aminobutyric acid, norepinephrine, and serotonin and the effects of drugs and diet on seizure susceptibility. Mice from six different genetic strains are pretreated with a drug or a particular type of diet: drugs used include glutamic acid, 5-hydroxytryptophan, reserpine, iproniazid, amino-oxyacetic acid, and diphenylhydantoin; diets are varied in phenylalanine, tyrosine, and pyridoxine content. Behavioral response to seizures induced by sound, pentylenetetrazol, or electricity is observed, and brain levels of biogenic amines are determined. Susceptibility to both audiogenic and electroconvulsive seizures has been found to vary among the six different strains of mice, while susceptibility among members of each strain is highly correlated.

213630 Sedvall, Goran C. Karolinska Institutet, Stockholm, Sweden **Chlorpromazine and brain catecholamine synthesis.** Psychopharmacology Bulletin. 11(2):60, 1975.

The effects of chlorpromazine and other phenothiazines, thioxanthenes, butyrophenones, and dibenzoazepines on brain dopamine and related substances are being studied in rats to elucidate the mechanism of action of these antipsychotic drugs. Results indicate that chlorpromazine accelerates brain dopamine synthesis partly by an indirect mechanism, presumably involving acceleration of nerve impulses in the nigrostriatal dopamine pathway as a result of dopamine receptor blockade. Results are compatible with the view that all antipsychotic drugs enhance tyrosine hydroxylation in brain dopamine neurons. Results of related studies suggest that the antipsychotic effects of neuroleptic agents may be related to interaction with limbic dopaminergic mechanisms; the impact on striatal mechanisms which are apparently involved in the production of extrapyramidal side-effects may also be significant in the induction of antipsychotic action.

213632 Shore, Parkhurst A. University of Texas, Southwestern Medical School, Dallas, TX **Mechanisms of storage and release of amines.** Psychopharmacology Bulletin. 11(2):61-62, 1975.

The role played by the biogenic amines in a wide variety of psychological processes and disease states, including mental illness, is being studied in animals. Amantadine, reserpine, tetrabenazine, metaraminol, and potassium are being used in various species to determine their effects on transport, storage, and release of biogenic amines, and results of preliminary studies are discussed. In related experiments, the effects of cocaine, desipramine, bretylium, debrisoqiun, and reserpine on adrenergic transmission are being investigated. Other studies suggest that alpha-meta-tyramine may be a false dopaminergic transmitter in the corpus striatum.

213633 Snyder, Solomon H. Johns Hopkins University School of Medicine, Baltimore, MD 21218 **Neurochemical actions of psychotropic drugs.** Psychopharmacology Bulletin. 11(2):62, 1975.

Neurotransmitters and related compounds in the nervous system and their interactions with psychotropic drugs are

being studied in various species to elucidate the nature of various neurohumoral receptors, including the glycine receptor, the nerve growth factor receptor, and the muscarinic cholinergic receptor. Studies are carried out in vivo and in vitro, applying both standard clinical procedures and newly developed assay techniques to determine the distribution and concentration of endogeneous substances and to test receptor responsiveness to psychoactive compounds. Results of studies of receptor binding and affinity for various compounds are included.

213685 Quadagno, David M.; Ho, George K. W. Department of Physiology and Cell Biology, University of Kansas, Lawrence, KS 66045 **The reversible inhibition of steroid-induced sexual behavior by intracranial cycloheximide.** Hormones and Behavior. 6(1):19-26, 1975.

Cycloheximide(Cyclo), an inhibitor of protein synthesis by a direct action on protein synthesis at the ribosomal level, was used to reversibly inhibit estrogen induced sexual receptivity. Cyclo was infused into the preoptic area (POA) of ovariectomized rats at varying times before, simultaneously with, and after subcutaneous estradiol benzoate (EB). All animals received 0.5mg progesterone (P) 36 hr after EB, and were tested for sexual receptivity 4-6 hr after P. When those animals that showed low levels of sexual behavior after Cyclo infusion were reprimed with EB and P 7 days later and presented with a male they showed high levels of sexual receptivity. Thus, the effect of Cyclo was reversible. Only Cyclo infusions into the POA (bilateral) and third ventricle, and unilateral POA infusions were without effect. 13 references. (Author abstract modified)

213855 Halfon, Neal; Goldowitz, Daniel; Glotzbach, Steven; Berger, Ralph. Division of Natural Sciences, University of California, Santa Cruz, CA 95064 **Decreased temporal variability in hippocampal theta rhythms of cats administered methylphenidate.** Behavioral Biology. 13(4):497-503, 1975.

Hippocampal theta activity, after an intraperitoneal injection of methylphenidate, was monitored in cats with chronically implanted hippocampal recording electrodes. Over a 90 minute control recording session, the hippocampal theta rhythm exhibited random fluctuations in activity levels. Following methylphenidate injections, the temporal variability of the theta rhythm was significantly reduced. Hypotheses are presented in relation to the hyperkinetic syndrome observed in children. 20 references. (Author abstract)

213987 Reid, John L.; Zivin, Justin A.; Foppen, Fredrik H.; Kopin, Irwin J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Catecholamine neurotransmitters and synthetic enzymes in the spinal cord of the rat.** Life Sciences (Oxford). 16(6):975-984, 1975.

Total catecholamines (CA), norepinephrine (NE) and small amounts of dopamine were measured in the spinal cord of rats by sensitive radiometric assays, and transmitter levels were correlated with dopamine-beta-hydryoxylase (DBH) and phenylethanolamine-N-methyl transferase (PNMT). There was a considerable disparity between levels of NE and those of total CA, suggestiing the presence of significant amounts of another CA in spinal cord. The demonstration of PNMT activity in spinal cord suggested that the CA could be epinephrine (E). The presence of E in spinal cord was confirmed by quantitative mass fragmentography. Pretreatment with intracisternal and intracerebroventricular 6-hydroxydopamine markedly reduced the contents of total CA, NE and DBH activity when compared to vehicle treated controls. In contrast, the levels of dopamine only fell to 50% of controls after 6-hydroxydopamine. It is concluded that, in addition to descending noradrenergic tracts, adrenergic neurons are present in the spinal cord. 26 references. (Author abstract modified)

214055 Marois, Maurice; Marois, Genevieve. Laboratoire d'histologie de la Faculte de Medecine Saint-Antoine, 27, rue Chaligny, F-75571 Paris Cedex 12 **/Psychotropic drugs, ovarian functions and mammary activity./** Drogues psychotropes, fonctions ovariennes et activite mammaire. Steroids and Lipids Research (Basel). 5(4):224-231, 1974.

The action of four psychotropic drugs (reserpine and three derivatives of phenothiazines) on ovarian function and mammary activity was studied in adult female rats. As with reserpine, the three phenothiazine derivatives were found to interrupt the cycle, allow the formation of a decidua, and, in most of the female rats, bring on lactation. Greater effects corresponded to greater doses. Uterus reaction was quicker and more constant, but less durable, than mammary gland reaction. Of the three phenothiazines, chlorpromazine was the least active, trifluoperazine was next active, and thioproperazine was the least toxic and the most active. 5 references. (Author abstract modified)

214062 Starke, Klaus; Endo, Takahiko; Taube, Hans Detlef. Pharmakologisches Institut, Klinikum der Universitat Essen, Hufelandstr. 55, D-4300 Essen, Germany **Pre- and postsynaptic components in effect of drugs with alpha-adrenoceptor affinity.** Nature (London). 254(5499):440-441, 1975.

Effects of drugs which activate alpha adrenoceptors were examined in studies on rabbit main pulmonary arteries, in which postsynaptic alpha adrenoceptors mediate vasoconstriction. Artery strips were superfused with Krebs-Henseleit solution containing propranolol, cocaine and corticosterone to block beta adrenoceptors and the neuronal - extraneuronal uptake of noradrenaline, respectively. Oxymetazoline preferentially activated presynaptic alpha adrenoceptors. Methoxamine behaved like phenylephrine; clonidine was shown to behave like oxymetazoline. Oxymetazoline and clonidine reduced, whereas phenyleprine and methoxamine enhanced neurogenic vasoconstriction. 12 references.

214109 Aeschbacher, Hans-Ulrich; Atkinson, Jeffrey; Domahidy, Beatrice. Nestle Products Technical Assistance Company Ltd., Biological Laboratories, 1350 Orbe, Switzerland **The effect of caffeine on barbiturate sleeping time and brain level.** Journal of Pharmacology and Experimental Therapeutics. 192(3):635-641, 1975.

Studies in rats were designed to determine whether the shortening of barbiturate sleeping time (ST) by caffeine was due to stimulation of the liver microsomal enzyme activity or to antagonism in the brain. Caffeine pretreatment shortened barbital induced ST, and coffee had an effect in direct proportion to its caffeine content. Decaffeinated coffee was without effect. To determine if shortening of ST was due to an interaction at the brain level, hexobarbital, which is metabolized by the liver, was used. Barbital was only negligibly metabolized in the liver. Pretreatment with caffeine shortened the hexobarbital ST even though the brain concentration of the latter was actually elevated. Caffeine pretreatment was also much less effective than phenobarbital pretreatment in stimulating the enzyme systems in the liver which metabolize hexobarbital, aminopyrine and ethylmorphine (in vitro). It is concluded that the caffeine stimulation of liver metabolism is a relatively minor factor in the shortening of barbiturate ST by caffeine in comparison to the brain interaction of these two drugs. 16 references. (Author abstract modified)

214110 Chiueh, C. C.; Moore, K. E. Dept. of Pharmacology, Michigan State University, East Lansing, MI 48824 **d-Amphetamine-induced release of "newly synthesized" and "stored" dopamine from the caudate nucleus in vivo.** Journal of Pharmacology and Experimental Therapeutics. 192(3):642-653, 1975.

In a study of d-amphetamine induced release of dropamine from the caudate nucleus, the lateral and third ventricles of anesthetized cats were perfused continuously with artificial cerebrospinal fluid (CSF) containing 3H-tyrosine and the perfusate was analyzed for 3H-catecholamines. The addition of d-amphetamine sulfate to the perfusing CSF for 2 hours, beginning 2 hours after the start of the 3H-tyrosine perfusion, caused an immediate increase in the efflux of 3H-dopamine. The efflux of this amine declined subsequently despite the continued presence of amphetamine in the CSF. The addition of alpha-methyltyrosine to the CSF concurrently with the d-amphetamine did not markedly alter the immediate increase but accelerated the subsequent decline in the efflux of 3H-dopamine. The addition of d-amphetamine to the 3H-tyrosine containing CSF at the start of perfusion immediately increased the efflux of 3H-dopamine, a response which was completely blocked by the presence of alpha-methyltyrosine in the CSF. Pretreatment of cats with reserpine effectively depleted the caudate nucleus of endogenous and 3H-dopamine but did not alter the ability of d-amphetamine to increase the efflux of 3H-dopamine. 50 references. (Author abstract modified)

214203 Davison, Meredith Ann. University of Oklahoma **The electrodermal response: neurophysiological and neuropharmacological characteristics. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-2967 HC$13.50 MF$5.00 72 p.

A ventrolateral brainstem pathway from which maximal electrodermal responses could be elicited was systematically explored in the cat by direct stimulation techniques. Reactive loci in this pathway extended from the rostral border of the posterior hypothalamus to the cervical cord. Sites stimulated were highly reactive, reproducible between Ss, and extremely stable. Stimulation of the ventrolateral extent of the medulla evoked similar, if not greater, responses in the decerebrate preparation. The primary area for integration of the electrodermal reflex was found in the lower mesencephalic/pontine region. Moderate doses of adrenergic stimulants caused a brief decline in the magnitude of the electrodermal response elicited by either central or peripheral stimulation. Propranolol blocked the depressive effect of isoproterenol, but neither propranolol nor phenoxybenzamine abolished the effects of epinephreine and norepinephrine. Once the brainstem pathway was determined and the basic characteristics of the electrodermal response were defined, direct (central and peripheral) and reflex activation of this sudomotor system were used as a model with which to study drug effects (reserpine and chlorpromazine) on the CNS. (Journal abstract modified)

214323 Wade, Lester A.; Katzman, Robert. Department of Neurology, Albert Einstein Medical College, Bronx, NY 10461 **Rat brain regional uptake and decarboxylation of L-DOPA following carotid injection.** American Journal of Physiology. 228(2):352-359, 1975.

Using the carotid injection technique, the regional uptake and decarboxylation of L-DOPA at the blood-brain barrier in the rat was studied. After a single intracarotid injection in the rat followed by decapitation 15 seconds later, the uptake of L-DOPA was measured relative to tritiated water injected simultaneously as a diffusible internal standard. A regional study showed that uptake operated at approximately the same rate in the various brain areas despite marked regional variation in catecholamine concentration. The decarboxylation of L-DOPA also occurred at a similar rate in all regions. These results support the hypothesis that L-DOPA movement into the brain occurs via a neutral amino acid transport mechanism common to cerebral capillaries of different regions of the brain. 44 references. (Author abstract)

214716 Crawford, I. L.; Connor, J. D. Dept. of Pharmacology, Milton S. Hershey Medical Center, Pennsylvania State University, Hershey, PA 17033 **Zinc and hippocampal function.** Journal of Orthomolecular Psychiatry (Regina). 4(1):39-52, 1975.

The relationship between zinc and hippocampal function is analyzed by correlating ontogenetic changes in hippocampal zinc with emerging cytomorphology in maturing rats, studying the effect of a zinc chelate on electrophysiologically evoked waves, and examining other endogenous substances which may be involved with zinc in synaptic function. In vivo studies in 10-20-day-old rats indicate that changes in localization and concentration of zinc may be related to granule cell morphogenesis and functional ontogeny. Analyses of hippocampal eletrophysiological waves following administration of dithizone indicate that zinc may be required for activating pyramidal cells through the mossy fiber pathway, and may contribute to a variety of cerebral physiopathologies via limbic connections. The location of glutamic acid and L-glutamic acid dehydrogenase in a hippocampal layer which contains notable portions of zinc suggests that zinc may subserve synaptic functions in neurotransmission. 79 references. (Author abstract modified)

215066 Jakoubek, B.; Kraus, M.; Erdosova, R.; Lat, J.; Dedicova, A. Institute of Physiology, Czechoslovak Academy of Sciences, Prague-Krc, 1083 Czechoslovakia **The effect of ACTH and diazepam, administered to infant rats on the body-growth curve and some endocrine parameters measured in adult age.** Activitas Nervosa Superior (Praha). 16(4):246-247, 1974.

At the 16th Annual Psychopharmacological Meeting, Jesenik, 1974, a paper was presented which reported the use of repeated injections of adrenocorticotropic hormone (ACTH) as a model of the activation of the hypophyseal adrenal system in very young rats; repeated injections of diazepam were used as a model of a suppression of this system. The effect of the postnatal administration of these drugs on the body growth curve, weights of some organs and the corticosterone production in adult age were reported. It was generally concluded that the changes in early infancy, induced by ACTH or diazepam, deeply affect the endocrine balance in adult age. 1 reference.

215069 Mayer, O. Institute of Pharmacology, Medical Faculty, Charles University, 30167 Plzen, Czechoslovakia **The effect of sodium gamma-hydroxybutyrate on the CNS of rats and mice.** Activitas Nervosa Superior (Praha). 16(4):250-251, 1974.

At the 16th Annual Psychopharmacological Meeting, Jesenik, 1974, a paper was presented which reported the effect of sodium gamma-hydroxybutyrate (GHB) on the central nervous system (CNS) of rats and mice in doses that were lower than anesthetic doses. The findings indicate that there is no definite inhibitory effect on the CNS. The circumstance that this is a substance occurring in the brain and that the inhibitory effect is not combined with an anticonvulsive one suggests that this substance should be classified psychopharmacologically. 6 references.

215076 Nikolova, M.; Stephanova, D.; Tchavdarov, D. Institut des recherches de chimie pharmaceutique, Zhelyo Voivoda 1-a, Sofia, Bulgaria **/Influence of tempidon on the EEG of cats at a single and repeated application/.** L'influence du tempidon sur l'EEG des chats dans l'experience aigue et chronique. Activitas Nervosa Superior (Praha). 16(4):264-268, 1974.

The mechanism of the action of tempidon (2,2,6,6-tetramethylpiperidon p-toluolsulphonate), a tranquilizing Bulgarian drug, on cortical activity, hypothalamus, ascendent reticular formation and nucleus ruber was studied in acute and chronic experiments on cats. Tempidon in therapeutic doses has a moderate depressive effect on the cerebral electrogenesis with a parallel synchronizing effect without a large deviation in the electroencephalogram findings. These changes were probably due to some decreasing effect on the activity of the ascendent reticular formation. 12 references. (Author abstract)

215159 Hosli, Elisabeth; Bucher, U. M.; Hosli, L. Dept. of Neurophysiology, Neurological Clinic of the University of Basel, Socinstrasse 55, CH-4051 Basel **Uptake of 3H-noradrenaline and 3H-5-hydroxytryptamine in cultured rat brainstem.** Experientia (Basel). 31(3):354-356, 1975.

Cellular location of the uptake of monoamines was examined in cultures made from the medulla oblongata and pons of fetal (18 days in utero) and newborn rats. Radiolabelled norepinephrine (3H-NE) and serotonin (3H-5-HT) were found to be taken up by the majority of brainstem cultures, accumulating in nerve fibers growing out from the explant into the outgrowth zones and taken up by a small proportion of neurons. Autoradiographic analysis indicates that labelled fibers form contacts with unlabelled neuronal cell bodies by "en passant" synapses. No difference was observed between cultures which were treated with monoamineoxidase inhibitor and untreated ones. It is concluded that there is a difference between the cellular localization of the uptake of monoamines, for which specific high affinity uptake systems constitute an important mechanism for termination of action, and that of amino acid transmitters where glial cells play a role in inactivation. 20 references.

215161 Goldman, H.; Fischer, R.; Nicolov, N.; Murphy, S. Dept. of Pharmacology, Wayne State Univ. School of Medicine, 540 E. Canfield Ave., Detroit, MI 48201 **Lysergic acid diethylamide affects blood flow to specific areas of the conscious rat brain.** Experientia (Basel). 31(3):328-330, 1975.

Various areas of the brain which might be altered by lysergic acid diethylamine (LSD) were examined by regional perfusion of the nervous system in conscious, unrestrained rats. Blood flow changes to the parietal and frontal cortex, the cerebellum, and the dorsal hippocampus appear to be related to behavioral effects. Findings with 2-methyl-LSD, 6-nor-LSD, and delta8,9-LSD, to which rats are not visibly responsive, reveal no changes in regional perfusion of the brain. Findings of increased blood flow to certain areas of the brain of conscious rats following LSD suggest that these relatively restricted responses are the result of tissue activity responses likely to be obscured by whole brain measurements or the use of anesthetics. 12 references.

215162 Krupp, P.; Wesp, M. Research Dept. Pharmaceuticals Division, Ciba-Geigy Limited, CH-4002 Basel **Inhibition of prostaglandin synthetase by psychotropic drugs.** Experientia (Basel). 31(3):330-331, 1975.

In vitro experiments were designed to determine whether compounds possessing neuroleptic, antidepressant and/or tranquilizing properties inhibit prostaglandin (PG) synthetase. All the psychotropic agents tested inhibited the conversion of arachidonic acid to PGE2, and the degree of inhibition was related to the concentrations used. The most potent were the tricyclic compounds chlorpromazine and clomipramine, followed by the ethaneanthracene derivatives maprotilene and benzoctamine. The tricyclic antidepressants amitriptyline, desipramine and imipramine were less active; haloperidol, a butyrophenone derivative, had only a very slight effect. 15 references.

215499 Nemtsov, A. V. Otdel psikhofarmakologii, Moskovskogo nauchno-issledovatel'skogo instituta psikhiatrii, Ministerstva zdravookhraneniya RSFSR, Moscow **/The action of chlorpromazine and triftasine on discharges of cortical neurons in rabbits after chronic administration of the drugs./** Deystviye aminazina i triftazina na razryady neyronov kory golovnogo mozga krolikov pri khronicheskom vvedenii preparatov. Zhurnal vysshey nervnoy deyatel'nosti imeni I. P. Pavlova (Moskva). 24(1):199-201, 1974.

The influence of chronic administration of chlorpromazine and triftazine on cortical neuron discharges was investigated in healthy rabbits with microelectrodes implanted in the visual cortex. Drugs were injected daily for 2 weeks in doses of 1mg/kg. Drug influence was measured by impulse frequency, the distribution of interpulse intervals and reaction to light flash stimulus. The most widespread effect of drug administration was found to be displacement of the mode of interpulse interval distribution. Neuroleptic drugs were, therefore, concluded to influence the cerebral informational processes. 9 references.

215600 Oleshansky, M. A.; Neff, N. H. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Rat pineal cyclic adenosine 3':5'-monophosphate phosphodiesterase activity: in vivo modulation by a beta adrenergic receptor.** Bethesda, MD, NIMH, 1975. 8 p.

Kinetic activity of cyclic adenosine 3',5'-monophosphate (cAMP) was studied in cAMP phosphodiesterase (PDE) of rat pineal gland by administration of l-isoproterenol. l-Isoproterenol treatment increased the activity of the low Km PDE of pineal by 40% within 1 hour and the activity returned to normal within 5 hours. The gain of activity was accompanied by a change of velocity maximum. Prior treatment of rats with dl-propranolol blocked the increase of PDE activity while treatment with phentolamine did not. Results suggest a direct relationship between cAMP concentrations and the increase of PDE activity. Tolerance to repeated doses of beta-receptor agonists might be explained by this mechanism. 26 references. (Author abstract modified)

215601 Romero, Jorge A.; Zatz, Martin, Axelrod, Julius. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Beta-adrenergic stimulation of pineal N-acetyltransferase: cyclic AMP stimulates both RNA and protein synthesis.** Bethesda, MD, NIMH, 1975. 13 p.

Because of the variations in lag period for induction of pineal N-acetyltransferase, the role of ribonucleic acid synthesis in the induction by catecholamines was studied. The data presented shows that N-acetyltransferase induction after activation of the beta-adrenergic receptor involves stimulation of both pretranscriptional and posttranscriptional events. Furthermore, cyclic adenosine 3',5'-monophosphate mediates either or

both of these actions of the beta-adrenergic receptor, depending upon the length of exposure of the rat to light or darkness. 12 references. (Author abstract modified)

215654 Guidotti, A.; Biggio, G.; Naik, N.; Mao, C. C. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **The in vivo regulation of cGMP content in rat cerebellum: a study of the action of taurine.** Bethesda, MD, NIMH, 1975. 11 p.

The effects of taurine glycine and gamma amino butyric acid (GABA) on the cerebellar cyclic guanisine monophosphate (cGMP) concentrations and on the elevation of cGMP elicited by harmaline, cold exposure or isoniazid injection in rat cerebellum were compared. Results show that taurine can interfere with the regulation of cerebellar cGMP content but its action differs from that of glycine and GABA. 23 references.

215664 Chopra, Y. M.; Dandiya, P. C. Department of Pharmacology, S. M. S. Medical College, Jaipur, India **The mechanism of the potentiating effect of antidepressant drugs on the protective influence of diphenhydramine in experimental catatonia. The role of histamine.** Pharmacology (Basel). 12(6):347-353, 1974.

The anticatatonic action of various antidepressants in moderate doses and their combination with subeffective doses of diphenhydramine was correlated with rat brain histamine levels. The catatonia was induced by perphenazine with a concomitant and remarkable increase in the brain histamine level. Diphenhydramine partially protected the animals from the increase in brain histamine and mitigated the catatonia. The antidepressants, i.e. monoamine oxidase inhibitors and tricyclic antidepressants, partially protected animals from both the increase in brain histamine and also the catatonia. The tricyclic antidepressants were, however, found to be more potent in both respects. The combination of subeffective doses of monoamine oxidase inhibitors and diphenhydramine was effective in terminating experimental catatonia and the elevation of brain histamine while tricyclic antidepressants failed. A relationship between the duration of protection against catatonia and brain histamine level due to antidepressants alone and their combination with diphenhydramine was observed. 23 references. (Author abstract)

215666 Cherksey, Bruce D.; Altszuler, Norman. Department of Pharmacology, New York University School of Medicine, New York, NY **On the mechanism of potentiation by morphine of thiopental sleeping time.** Pharmacology (Basel). 12(6):362-371, 1974.

In a study of morphine potentiation of thropental sleeping time, it was found that injection of thiopental sodium, i.p.,into normal rats produced a prompt sleep. Injection of morphine sulphate itself produced only mild sedation but prolonged the thiopental induced sleep to 50 and 67.3min, respectively. At 1 min after onset of sleep the brain thiopental concentration in morphine pretreated animals was significantly lower than in control animals. The latter also awoke with higher brain thiopental concentrations; the morphine pretreated animals slept for a longer time despite lower brain theopental concentration. Distribution of thiopental in several tissues at various time periods following injection of thio;ental revealed some time related quantitative differences between the two groups but a similar qualitative pattern. It is suggested that morphine lowers the brain threshold for thiopental induced sleep. 11 references. (Author abstract modified)

215683 Paalzow, Gudrun; Paalzow, Lennart. Department of Pharmaceutical Pharmacology, University of Uppsala, Uppsala, Sweden **Antinociceptive action of oxotremorine and regional turnover of rat brain noradrenaline, dopamine and 5-HT.** European Journal of Pharmacology (Amsterdam). 31(2):261-272, 1975.

The antinociceptive actions of oxotremorine and regional turnover of rat brain noradrenaline, dopamine and 5-hydroxytryptamine (5-HT) were studied. 1-Tryptophan, PCPA, alpha-methyl-p-tyrosine, 1-Dopa pimozide and lysergic acid diethylamide (LSD) 25 did not affect the antinociceptive activity of oxotremorine. Oxotremorinde did not change the endogenous brain concentrations of noradrenaline and dopamine or 5-HT but decreased that of 5-hydroxyindole acetic acid (5-HIAA) in all brain regions at the time of maximal analgesia. The decrease of 5-HIAA was still present after pretreatment with probenecid. After inhibition of tyrosine hydroxylase, oxotremorine accelerated the depletion of dopamine in telencephalic cortex during maximal antinociceptive activity and of noradrenaline in all brain regions at a time when this activity had vanished. Atropine significantly antagonized the analgesic activity of oxotremorine. It is concluded that oxotremorine antinociceptive activity in the rat is related to a cholinergic component, while a monoaminergic component is not directly involved. 52 references.

215686 Nose, Takashi; Takemoto, Hiroshi. Department of Pharmacology, Safety Research Laboratory, Tanabe Seiyaku Co., Ltd., Yodogawa-ku, Osaka, Japan **The effect of penfluridol and some psychotropic drugs on monoamine metabolism in central nervous system.** European Journal of Pharmacology (Amsterdam). 31(2):351-359, 1975.

In a study of monoamine metabolism in central nervous system, five neuroleptics: penfluridol, haloperidol, chlorpromazine, pimozide and oxypertine, and two benzodiazepine minor tranquilizers; chlordiazepoxide and diazepam, were studied in mice and rats. When the drugs were injected i.p. in mice, all neuroleptics increased the brain homovanillic acid (HVA) concentration but two benzodiazepines did not change it. Of the drugs tested, only pimozide increased the brain level of 5-hydroxyindoleacetic acid. Pnefluridol accelerated the turnover rate of brain dopamine (DA), whereas haloperidol accelerated both DA and noradrenaline turnover rates. In rats, oral administration of penfluridol caused an increase in the striatal HVA and 93,4-dihydroxyphenylacetic acid which persisted longer than that following haloperidol. It is concluded that the effect of penfluridol on DA metabolism resembles that of typical neuroleptic compounds and penfluridol acts only on DA neurons as a long acting DA receptor blocker. 23 references. (Author abstract modified)

215687 Simpson, Lance L. Department of Pharmacology, College of Physicians and Surgeons, Columbia University, New York, NY **Blood pressure and heart rate responses evoked by d- and l-amphetamine in the pithed rat preparation.** Journal of Pharmacology and Experimental Therapeutics. 193(1):149-159, 1975.

Isomers of amphetamine were tested for their ability to evoke changes in the spontaneous motor behavior of rats. d-Amphetamine increased activity. Both d- and l-amphetamine were also compared for their pressor and tachycardic activity in pithed rats. The doses of amphetamine tested were identical to those which produced changes in behavior. d-Amphetamine was approximately 5-fold more potent than l-amphetamine in evoking pressor responses and approximately 3-fold more potent in evoking tachycardic responses. The two isomers dif-

fered little in their ability to block norepinephrine uptake into heart. The inability of cocaine to evoke responses were related to the marked reduction in norepinephrine turnover and release in pithed animals. It was concluded that differences in potency between d-amphetamine and l-amphetamine cannot be explained on the basis of blockade of norepinephrine uptake. The difference may relate to evoked release of amine. 28 references. (Author abstract modified)

215688 Hanbauer, I.; Kopin, I. J.; Guidotti, A.; Costa, E. Section of Biochemical Pharmacology, Hypertension Endocrine Branch, National Heart and Lung Institute, Bethesda, MD 20014 **Induction of tyrosine hydroxylase elicited by beta adrenergic receptor agonists in normal and decentralized sympathetic ganglia: role of cyclic 3',5'-adenosine monophosphate.** Journal of Pharmacology and Experimental Therapeutics. 193(1):95-104, 1975.

The effects of subcutaneous injection of l-epinephrine dopamine or l-norepinephrine administered with phenoxybenzamine to block alpha adrenergic effects were studied in rats. The drugs increased the cyclic 3',5'-adenosine monophosphate (cAMP) content in superior cervical ganglia (SCG) of rats. The increase is highest after l-epinephrine and dopamine and is barely detectable after l-norepinephrine; it last longer than 2 hours after l-epinephrine, about 30 minutes after dopamine and is fleeting after l-norepinephrine. The duration of the increase in cAMP elicited by l-epinephrine in SCG of rats is dose related. Furthermore, when the cAMP increase lasts longer than 90 minutes, 48 hours later the tyrosine hydroxylase (TH) activity in SCG is increased. l-Epinephrine induces TH in decentralized ganglia. dl-Propranolol injected 30 minutes before l-isoproterenol blocks the increase of cAMP content and the delayed induction of TH activity in SCG. The elevation of TH activity elicted in SCG by beta adrenergic receptor agonists is always preceded by an increase of cAMP concentration lasting 90 minutes or longer. 27 references. (Author abstract modified)

215690 Uretsky, Norman J.; Chase, Gerald J.; Lorenzo, Antonio V. Neurology Research Lab., Childrens Hospital Medical Center, 300 Longwood Ave., Boston, MA 02115 Medical Center, Boston, MA **Effect of alpha-methyldopa on dopamine synthesis and release in rat striatum in vitro.** Journal of Pharmacology and Experimental Therapeutics. 193(1):73-87, 1975.

The effect of alpha-methyldopa and alpha-methyldopamine (MDA) on the rate of hydroxylation of radioactive tyrosine was studied in striatal slices from rat brain. This was done by measuring the formation of 3H-H2O as well as the accumulation of 3H-dopamine (3H-DA) from L-3, 5-3H-tyrosine. Methyldopa, at tissue concentrations similar to those found in vivo after systemic administration, produced a decrease in both 3H-H2O and 3H-DA. The inhibitory effect of methyldopa on 3H-H2O formation was not reduced by the addition of brocresine, which prevents the formation of MDA. The effects of methyldopa and alpha-MDA on the release of 3H-DA that had been taken up into brain slices, was also studied. These results, as well as the close similarity between the percent reduction of 3H-H2O formation and tissue 3H-DA levels, suggest that methldopa decreases tissue levels of dopamine by inhibiting tyrosine hydroxylase activity in DA neurons. 44 references. (Author abstract modified)

215691 Kalisker, Albert; Waymire, Jack C.; Rutledge, Charles O. Lab. of Biochemical Pharmacology, Children's Asthma Research Institute and Hospital, Nat'l. Asthma Ctr., 1999 Julian St., Denver, CO 80204 **Effects of 6-hydroxydopamine and reserpine on amphetamine-induced release of norepinephrine in rat cerebral cortex.** Journal of Pharmacology and Experimental Therapeutics. 193(1):64-72, 1975.

The effects of 6-hydroxydopamine and reserpine on amphetamine induced release of norepinephrine were studied in the rat cerebral cortex. Amphetamine released 3H-norepinephrine from rat cerebral cortex tissue which had previously accumulated the 3H-amine. Destruction of noradrenergic nerve endings by pretreatment of the rats with 6-hydroxydopamine inhibited the accumulation of 3H-norepinephrine by the tissue and reduced the proportion of the 3H-amine which was released by amphetamine. Inhibition of storage of 3H-norepinephrine witin nerve endings by pretreatment of the animals with reserpine also reduced accumulation of 3H-norepinephrine did not reduce the proportion of the accumulated 3H-amine which was released by amphetamine. The experiments indicate that amphetamine releases 3H-norepinephrine primarily from storage sites within central adrenergic nerve endings. An analysis of the time course of release from tissues of rats treated with reserpine suggests that amphetamine is equally capable of release from tissues of rats treated with reserpine suggests that amphetamine is equally capable of releasing 3H-norepinephrine from granular sites which are susceptible to reserpine and from reserpine insensitive sites. 45 references. (Author abstract modified)

215692 Breese, George R.; Cott, Jerry M.; Cooper, Barrett R.; Prange, Arthur J., Jr.; Lipton, Morris A.; Plotnikoff, Nicholas P. 226 Biological Sciences Research Center, University of North Carolina, School of Medicine, Chaptel Hill, NC 27514 **Effects of thyrotropin-releasing hormone (THR) on the actions of pentobarbital and other centrally acting drugs.** Journal of Pharmacology and Experimental Therapeutics. 193(1):11-22, 1975.

In a study of the actions of pentobarbital in mice, throtropin releasing hormone (TRH) was found to antagonize pentobarbital induced sleeping time and hypothermia. White 3 to 100mg/kg of TRH reduced pentobarbital sleeping time when administered prior to the barbiturate, a dose response relationship to TRH could not be established. Thyrotropin or L-triiodothyronine did not imitate and hypophysectomy did not reduce the effects of TRH, indicating that the pituitary is not essential for its antagonism of pentobarbital. Intracisternally administered TRH also reduced pentobarbital sleeping time and hypothermia, but melanocyte stimulating hormone release inhibiting factor and somatostatin administering by this route did not. While reduction of pentobarbital sleeping time by TRH could not be attributed to an affect on monoamine systems or to deamidated TRH, this action was reduced by intracisternally administered atropine, suggesting that cholinergic mechanisms may contribute to the effects of TRH. Thus, the results provide evidence that TRH acts on brain independent of an effect on the pituitary. 31 references. (Author abstract modified)

215702 Blondaux, Chantal; Buda, Michel; Petitjean, Francoise; Pujol, Jean-Francois. Departement de Medecine Experimentale, Universite Claude Bernard, 8, Avenue Rockefeller, 69008 Lyon, France **/Hypersomnia by isthmic lesion in the cat. I. Study of the metabolism of cerebral monamines./** Hypersomnie par lesion isthmique chez le chat. I. Etude du metabolisme des monoamines cerebrales. Brain Research (Amsterdam). 88(3):425-437, 1975.

In a study of metabolism of cerebral monoamines, a significant increase of 5-hydroxytryptamine (5-HT) synthesis was observed in several areas of the cat brain 24 h after the bilateral

destruction of the dorsal noradrenergic bundle in the isthmus. This stimulation of the synthesis was simultaneously observed at the level of serotoninergic cell bodies (anterior part of the raphe system) and of 5-HT terminals (cortex, thalamus, mesencephalon, medulla oblongata). A significant decrease of 5-HT synthesis was found in the caudal part of the raphe and in the hypothalamus. The possibility of a catecholaminergic control of 5-HT synthesis by neurons passing through the isthmus is discussed. In the same experimental conditions, an important decrease of endogenous dopamine content without any subsequent change of noradrenaline concentration was observed in the thalamus, the geniculate body and the pons. This important decrease could be due to a greater utilization of dopamine into hypothetical dopaminergic terminals localized in these structures. 30 references. (Author abstract)

215703 Petitjean, Francoise; Sakai, Kazuya; Blondaux, Chantal; Jouvet, Michel. Departement de Medecine Experimentale, Universite Claude Bernard, 8, Avenue Rockefeller, 69373 Lyon, France /**Hypersomnia by isthmic lesion in the cat. II. Neurophysiological and pharmacological study.**/ Hypersomnie par lesion isthmique chez le chat. II. Etude neurophysiologique et pharmacologique. Brain Research (Amsterdam). 88(3):439-453, 1975.

The bilateral destruction of the region of the dorsal norepinephrine bundle in the isthmus or in the mesencephalon was studied. A significant increase of both paradoxical sleep (PS) and of slow wave sleep (SWS) was found. The increase of PS lasted for 4-5 days while the increase of SWS lasted at least 8-10 days. The same phenomenon was observed after total hypophysectomy. Control lesions effectuated in the isthmus outside the area of the dorsal norepinephrine bundle did not affect significantly the sleep - waking cycle. Pretreatment with p-chlorophenylalanine suppressed the increase of sleep if the lesion was effectuated at the time of maximum insomnia, while a significant increase of PS still observed if the lesion was made at the time of the recovery of sleep. The mechanisms of this hypersomnia are discussed in light of the biochemical results showing an increase of the biosynthesis of serotonin in the rostral raphe system. It is postulated that some neurons of the dorsal norepinephrine bundle might tonically control the activity of the raphe system. 28 references. (Author abstract modified)

215705 Woodson, Paul B. J.; Schlapfer, Werner T.; Tremblay, Jacques P.; Barondes, Samuel H. Department of Neuroscience, School of Medicine, University of California at San Diego, La Jolla, CA 92037 **Cholinergic agents affect two receptors that modulate transmitter release at a central synapse in Aplysia californica.** Brain Research (Amsterdam). 88(3):455-474, 1975.

During trains of stimulation which produced depression followed by facilitation of excitatory postsynaptic potentials, the effects of a large number of agents known to affect cholinergic transmission in Aplysia californica were studied. The agents could be divided into four classes: 1) agents having no effect upon transmission at the cholinergic function of a central synapse; 2) agents of a class typified by curare, which depressed all excitatory postsynaptic potentials (EPSP); 3) agents typified by acetylcholine and carbachol (ACh class) which reduced the fractional release of transmitter; 4) agents typified by trimethidinium (trimethidinium class) which appeared to act by reducing the rate of transmitter supply into the readily releaseable store. Neither the ACh class nor the trimethidinium class produced selective effects on different pulses in the train by changes in the postsynaptic membrane potential or membrane resistance. 33 references. (Author abstract modified)

215711 Haubrich, D. R.; Goldberg, M. E. Department of Pharmacology, Squibb Institute for Medical Research, Princeton, NJ 08540 **Homovanillic acid concentration in rat brain: effect of a choline acetyltransferase inhibitor and comparison with cholinergic and dopaminergic agents.** Neuropharmacology (Oxford). 14(3):211-214, 1975.

The effects of the administration to rats of either atropine sulphate or 4-(1-naphthylvinyl) pyridine HCl, an inhibitor of choline acetyltransferase were examined. The drugs decreased the concentration of homovanillic acid in the corpus striatum by 50% as measured 1 hr later. The decrease in homovanillic acid induced by administration of either agent was prevented by pretreatment with either pilocarpine HCl or eserine sulphate. Administration of apomorphine HCl or (+)-amphetamine sulphate also lowered the concentration of homovanillic acid. In contrast to the effects produced by atropine or naphthylvinyl pyridine, however, the decrease in homovanillic acid induced by treatment with either apomorphine or amphetamine was not reversed by pretreatment with either pilocarpine or eserine. Administration of either mecamylamine HCl, atropine methylnitrate or neostigmine methylsulphate had no effect on the level of homovanillic acid. These results suggest that naphthylvinyl pyridine possesses central anticholinergic activity similar to that of atropine. Furthermore, the cholinergic effect on the metabolism of dopamine in the corpus striatum appears to be mediated via muscarinic receptors in the central nervous system. 17 references. (Author abstract)

215712 Baum, T.; Shropshire, A. T. Cardiovascular Pharmacology Section, Wyeth Laboratories Inc., Radnor, PA 19087 **Inhibition of efferent sympathetic nerve activity by 5-hydroxytryptophan and centrally administered 5-hydroxytryptamine.** Neuropharmacology (Oxford). 14(3):227-233, 1975.

The role of sympathetic outflow in the cardiovascular response to 5-hydroxytryptophan (5-HTP) was examined. Intravenous injection of 5-HTP after peripheral decarboxylase inhibition resulted in a progressive reduction in blood pressure and heartrate in anesthetized cats. Spontaneous electrical activity of the cardiac, renal and splanchnic nerves also decreased in a dose related fashion. More direct administration of 5-HTP, as well as 5-hydroxytryptamine, to the brain via a lateral ventricle also produced a fall in pressure, heartrate and sympathetic nerve activity. These experiments indicate that the overall actions of 5-HTP on the central nervous system result in a diminution of sympathetic outflow leading to a reduction of blood pressure and heartrate and thus resemble the effects of L-DOPA. The actions of 5-hydroxytryptamine are consistent with the hypothesis that it mediates the response to 5-HTP. 32 references. (Author abstract modified)

215723 Fukuda, T.; Araki, Y.; Takishita, S.; Koga, T. Department of Pharmacology, Faculty of Medicine, Kyushu University, Fukuoka 812, Japan **Correlation between brain monoamine levels and postictal coma following electroshock.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 213(1):58-63, 1975.

Duration of postictal coma following maximal electroshock seizure and monoamine levels in the whole brain were measured in mice. Pretreatment with intraperitoneal alpha-methyl-p-tyrosine (MT), 5-hydroxytryptophan (5-HTP), or intraventricular 6-hydroxydopamine (6-OHDA) prolonged the coma duration, whereas p-chlorophenylalanine (PCPA) did not affect

the coma, and L-DOPA tended to shorten the coma and counteracted the effect of MT. When the shock was repeated five times with 1 hour intervals, the duration of coma was progressively increased, being accompanied by elevated serotonin (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) levels in the brain. In the MT treated group, a striking parallelism was remarked between coma prolongation and norepinephrine (NE) or dopamine (DA) reduction. These data suggest that prolongation of postictal coma is correlated with reduced NE and DA levels and/or with elevated 5-HT and 5-HIAA levels in the brain. 11 references. (Author abstract)

215724 Moore, R. H.; Demetriou, S. K.; Domino, E. F. Department of Pharmacology, Lafayette Clinic, Detroit, MI 48207 **Effects of iproniazid, chlorpromazine and methiothepin on DMT-induced changes in body temperature, pupillary dilatation, blood pressure and EEG in the rabbit.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 213(1):64-72, 1975.

The effects of i.v. N,N-dimethyltryptamine (DMT) were studied on arterial blood pressure, rectal temperature, pupil size and the electroencephalogram of the rabbit. DMT altered these parameters in a dose related manner causing increased blood pressure, hyperthermia, pupillary mydriasis and activation of the electroencephalogram. Pretreatment with the monoamine oxidase inhibitor, iproniazid, prolonged the effects of DMT, while pretreatment with chlorpromazine or methiothepin attenuated these actions of DMT. 25 references. (Author abstract)

215725 Pugsley, T. A.; Lippmann, W. Biochemical Pharmacology Department, Ayerst Research Laboratories, Montreal, Quebec, Canada **Effects of taclamine (AY-22,214), a new psychoactive agent, on catecholamine and serotonin metabolism.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 213(1):73-87, 1975.

The effects of a new psychopharmacologically active agent taclamine (AY-22,214 (AY) (a dibenzocycloheptaisoquinoline)) on noradrenaline (NA), dopamine (DA) and serotonin (5-HT) turnover in the brains of normal and/or stressed animals were determined by the use of both nonisotopic and isotopic techniques; a comparison with chlordiazepoxide (CL) was carried out. Both AY and CL antagonized the increase in NA and 3H-NA turnover due to immobilization stress in whole, and selected regions, of the rat brain. AY, unlike CL, did not decrease 3H-NA turnover in brains of nonstressed animals. AY did not alter 5-HT turnover. CL decreased 14C-5-HT turnover in regions of rat brain. Neither AY nor CL affected the 5-HT uptake in the mouse brain. It is concluded that AY appears to exhibit both similarities and differences to CL with regard to its effects on biogenic amine turnover. 36 references. (Author abstract)

215726 Davis, W. M.; Borgen, L. A. Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Tolerance development to the effect of delta9-tetrahydrocannabinol on conditioned behavior: role of treatment interval and influence of microsomal metabolism.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 213(1):97-112, 1975.

The importance of frequency of administration in the development of tolerance to delta9-tetrahydrocannabinol (THC) was studied in rats, with repeated administration of the drug prior to behavioral test sessions at 1, 3, 7 or 14 day intervals. Partial tolerance was seen to develop to the depressant effects of THC on food motivated performance on a variable interval 60 sec (VI 60) schedule of reinforcement. The tolerance was most evident with the most frequent exposure to the drug. Phenobarbital pretreatment for 7 days blocked the acute behavioral depressant effect of 4mg/kg of THC and appeared to enhance the development of tolerance. A metabolic mechanism of tolerance development was suggested by the data. 40 references. (Author abstract modified)

215727 Moore, R. H.; White, R. P. Department of Pharmacology, Lafayette Clinic, Detroit, MI 48207 **Central anticholinergic actions of doxepin in rabbits.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 213(1):113-120, 1975.

Neuropharmacological effects of doxepin were studied in rabbits to reveal fundamental actions which might explain its clinical efficacy. The results indicate that central effects of this compound are similar to those reported for atropine and the tricyclic antidepressants. Doxepin produced mydriasis and electroencephalogram (EEG) synchrony without producing overt signs of sleep. It inhibited in a dose related manner the EEG activation produced by physostigmine. It inhibited the EEG, but not behavioral, effects of methamphetamine. Doxepin enhanced some of the behavioral effects of methamphetamine, as does atropine. 22 references. (Author abstract)

215733 Yarbrough, G. G. Department of Psychology, University of Saskatchewan, Saskatoon, Saskatchewan, Canada **Actions of acetylcholine and atropine on cerebral cortical neurons in chronically morphine-treated rats.** Life Sciences. 15(8):1523-1529, 1974.

In rats receiving a daily injection of increasing doses of morphine for 25-29 days, the sensitivity of cerbral cortical neurons to acetylcholine (ACh) and the ability of atropine to antagonize ACh effects were examined. While the responses of neurons to ACh were qualitatively and quantitatively similar between morphinized and control animals, there was a marked reduction in the efficacy of atropine in blocking ACh effects in the morphine treated rats. 11 references. (Author abstract)

215734 Wiesel, Frits-Axel; Alfredsson, Gunnel; Likwornik, Victor; Sedvall, Goran. Division of Neuropsychopharmacology, Department of Pharmacology, Karolinska Institutet, S-104 01 Stockholm, Sweden **A relation between drug concentrations in brain and striatal homovanillic acid levels in chlorpromazine treated rats.** Life Sciences. 16(7):1145-1156, 1975.

Levels of homovanillic acid in striatum and chlorpromazine in brain and plasma of rats after acute and chronic treatment were determined by mass fragmentography. A significant positive correlation was found between the striatal homovanillic acid level and the chlorpromazine concentration in brain after acute as well as chronic treatment. A significant relation was also obtained between the homovanillic acid level in striatum and the chlorpromazine content of plasma after acute but not chronic treatment. After chronic treatment the drug concentration - effect relationship was significantly displaced to the right, which may indicate the development of pharmacodynamic tolerance to the effect of the drug. 21 references. (Author abstract)

215756 Heikkila, Richard E.; Orlansky, Herbert; Cohen, Gerald. Mount Sinai School of Medicine, Department of Neurology, Annenberg Building, Fifth Ave. at 100th St., New York, NY 10029 **Studies on the distinction between uptake inhibition and release of (3H)dopamine in rat brain tissue slices.** Biochemical Pharmacology (Oxford). 24(8):847-852, 1975.

The classification of drugs as either uptake inhibitors or releasing agents for biogenic amines was evaluated with rat brain tissue slices (neostriatum and cortex), using (3H)dopamine and the following compounds: potassium chloride, tyramine, d-amphetamine and l-amphetamine, cocaine, amantadine, desipramine, amitriptyline, nortriptyline and protriptyline. L-Dopa also caused release of (3H)serotonin and an inhibition of (3H)serotonin accumulation. Whenever a releasing action was observed, there was always a diminution in the amount of (3H)amine accumulation and this action was at least equal in magnitude to the percent released. Cocaine was an example of a pure uptake inhibitor; it did not evoke a releasing action at concentrations where a powerful uptake inhibition was seen. It was possible to conclude that, in the tissue slice system, an experimentally observed release was real, whereas a releasing action evoked an apparent inhibition of uptake equal in magnitude to the releasing action. The data indicate that, in the neostriatum, all of the drugs studied except cocaine were pure releasing agents and that drugs previously designated as uptake inhibitors were releasing agents. In the cortex, strong inhibition of uptake without significant releasing action was evident for many of the drugs. 17 references. (Author abstract modified)

215757 Antonaccio, M. J.; Robson, R. D. Research Department, Pharmaceuticals Division, Ciba-Geigy Corp., Summit, NJ 07901 **Centrally-mediated cardiovascular effects of 5-hydroxytryptophan in MAO-inhibited dogs: modification by autonomic antagonists.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 213(2):200-210, 1975.

In a study of monoamine oxidase (MAO) inhibited dogs, 5-hydroxytryptophan (5-HTP), either 5 or 10mg/kg, caused hypotension with variable effects on heartrate. Reflex responses to bilateral carotid artery occlusion (BCO) were greatly inhibited by 5-HTP. The hypotensive effects were markedly inhibited by cerebral and extracerbral decarboxylase inhibition with RO 4-4602 and the inhibition of BCO was delayed. Left ventricular pressure and dP/dt were reduced, but cardiac output was maintained by an increase in stroke volume. Hypotension was due predominantly to decreased peripheral resistance. The hypotensive action of 5-HTP was abolished or greatly attenuated after pretreatment with either yohimbine or methysergide, but was unaffected by haloperidol. These results indicate that cerebral decarboxylation and formation of serotonin are responsible for the hypotension after 5-HTP in MAO inhibited dogs. 30 references. (Author abstract modified)

215980 French, Samuel W.; Palmer, Douglas S.; Narod, Mary E. Department of Pathology, University of British Columbia, Vancouver, British Columbia **Effect of withdrawal from chronic ethanol ingestion on the cAMP response of cerebral cortical slices using the agonists histamine, serotonin, and other neurotransmitters.** Canadian Journal of Physiology and Pharmacology (Ottawa). 53(2):248-255, 1975.

The effect of ethanol withdrawal on the cAMP response of cerebral cortical brain slices was studied. The CAMP response was evoked in vitro by various neurotransmitters including norepinephrine (NE), histamine, serotonin, dopamine, acetylcholine, and gamma-aminobutyric acid (GABA). The cAMP response to NE and histamine was enhanced by ethanol withdrawal. Serotonin evoked a cAMP response in the brain slices from ethanol withdrawal rats but not in pair fed controls. The histamine and serotonin evoked responses were blocked by chlortripolon and methysergide, respectively. The responses to histamine and serotonin were also blocked by alpha-a0drenergic and beta-adrenergic antagonists. a GABA inhibited the NE stimulated cAMP response through the hyperpolarizing action of GABA. The results support the hypothesis that ethanol withdrawal induces a nonspecific postjunctional supersensitivity. Involvement of a partial depolarization of the receptor membrane is postulated. 29 references. (Author abstract modified)

216968 Carlsoo, B.; Danielsson, A.; Marklund, S.; Stigbrand, T. Departments of Histology and Physiological Chemistry, University of Umea, S-901 87 Umea, Sweden **Inhibition of catecholamine and 5-hydroxytryptamine induced enzyme secretion from the guinea-pig submandibular gland by 2-bromo-D-lysergic acid diethylamide.** Experientia (Basel). 31(4):395-397, 1975.

An experiment testing the inhibitory characteristics of 2-bromo-D-lysergic acid diethylamide (LSD) on catecholamine and 5-hydroxytryptamine (5-HT) induced enzyme secretion in the guinea-pig submandibular gland in vitro is reported. Gland fragments from 3-month-old, 300 gram guinea-pigs were incubated, treated with a combination of dibutyryl cyclic-AMP (DBcAMP) and theophylline, noradrenaline, adrenaline, dopamine and 5-HT. LSD inhibited not only peroxidase and amylase induced by 5-HT, but also by the other drugs listed with the exception of the DBcAMP in combination with theophylline. It is concluded that LSD cannot be considered as a specific 5-HT antagonist in salivary glands. 16 references.

217005 Leonov, B. V.; Limantsev, A. V.; Persianinov, L. S. Vsesoyuznyy nauchno-issledovatel'skiy institut akusherstva i ginekologii MZ SSSR, Moscow **/The protective effect of serotonin against the inhibitory action of chlorpromazine on thermembrane potential of stage 2 blastomeres of mouse embryos in vitro./** Zashchitnyy effekt serotonina ot depolyarizuyushchego vliayaniya aminazina na membrannyy potentsial embrionov myshey in vitro, nakhodyashchikhsya na stadii 2 blastomerov. Byulleten' eksperimental'noy biologii i meditsiny (Moskva). 79(1):41-43, 1975.

The influence on the embryos of mice during early embryogenesis of aminazine, serotonin and prostaglandin F2alpha on membrane potential was investigated in vitro. Membrane potential was measured with microelectrodes. Chlorpromazine was found to induce a strong decrease in membrane potential; serotonin and prostaglandin F2alpha did not affect membrane potential. Serotonin proved to be effective in preventing the inhibitory action of chlorpromazine on membrane potential; prostaglandin F2alpha, however, was unable to forestall the chlorpromazine action. 10 references. (Journal abstract modified)

217065 Zavodskaya, I. S.; Migas, E. A.; Bul'on, V. V. Laboratoriya eksperimental'noy farmakologii, Leningrad **/The effect of ethymizol on the content of cyclic 3',5'-adenosine monophosphate in brain tissue./** Vliyaniye etimizola na soderzhaniye tsiklicheskogo 3',5'-adenozinmonofosfata v tkani mozga. Byulleten' eksperimental'noy biologii i meditsiny (Moskva). 79(3):54-56, 1975.

The influence of ethymizol on the level of cyclic 3',5'-adenosine monophosphate (cAMP) in brain tissue was investigated in rats. An enzymatic method of cAMP determination showed a more than doubled cAMP increase in the brain tissue 20 minutes after intraperitoneal injections of ethymizol. Changes in cerebral carbohydrate metabolism typical of cAMP increased, i.e.,the glycogen level was reduced and the glucose level increased. Mechanisms of ethymizol action were concluded to be related to an increase in cAMP formation in the brain tissue. 10 references. (Journal abstract modified)

217067 Kvachadze, D. A. Tbilisskiy gosudarstvennyy, Meditsinskiy institut, Tbilisi, U.S.S.R. **/The effect of some neurotropic drugs on the phasic changes of arterial pressure evoked by stimulation of the cerebellar fastigal nucleus./** Vliyaniye nekotorykh neyrotropnykh sredstv na fazovyye sdvigi arterial'nogo davleniya vyzvannyye stimulyatsiyey krovel'nogo yadra mozzhechka. Soobshcheniya akademii nauk gruzinskoy SSR (Tbilisi). 77(1):177-179, 1975.

The influence of some neurotropic drugs on vascular - motor reactions elicited by local stimulation of the cerebellar fastigial nucleus was investigated in cats. The following parameters were used to determine the character of the vascular - motor reaction: latent period; amplitude of response; steepness of rise or fall of blood pressure; length of reaction. Hexenal, aminazine and pyperoxan were found to cause a considerable diminution of pressor effects resulting for fastigial nucleus stimulation. The influence of the analeptid drugs, i.e. corasol and caffeine, was found to depend upon the preferential localization of the action of the preparations. The inhibitory effect of aminazine and pyperoxan was concluded to show the existence of a direct fastigio - hypothalamic pathway in addition to the ordinary channels of fastigial vascular - motor effects. 7 references. (Journal abstract modified)

217214 Liberman, S. S.; Egorova, E. F.; Sharova, S. A. Vsesoyuznogo nauchno-issledovatel'skogo khimiko-farmatsevticheskogo instituta im. S. Ordzhonikidze, Moscow **/The influence of tricyclic antidepressants, azaphen and imizine on blood sugar concentration changes produced by epinephrine and serotonin.** Vliyaniye tritsiklicheskikh antidepressantov azafena i imizina na izmeneniye kontsentratsii sakhara krovi, vyzyvayemoye adrenalinom i serotoninom. Farmakologiya i Toksikologiya (Moscow). 37(1):18-21, 1974.

The effect of tricyclic antidepressants on blood sugar concentration changes produced by epinephrine and serotonin was investigated in rats and rabbits. Neither azaphen nor imizine was found to exert any direct influence on blood sugar concentration; both, however, increased the effect of epinephrine and serotonin on blood sugar concentration. Effective azaphen doses were two to four times as high as those of imizine. Repeated daily administration of azaphen did not change its potentiating action, but repeated doses of imizine yielded more prounced effects in rabbits. In both rats and rabbits, imizine more strongly influenced epinephrine activity, while azaphen was more influential in serotonin activity. 8 references. (Journal abstract modified)

217355 von Hungen, Kern; Roberts, Sidney; Hill, Diane F. Brain Research Inst., Univ. of California Ctr. for the Health Sciences, Los Angeles, CA 90024 **Serotonin-sensitive adenylate cyclase activity in immature rat brain.** Brain Research (Amsterdam). 84(2):257-267, 1975.

Cell free preparations from superior and inferior colliculi of very young rats which contained adenylate cyclase systems responsive to serotonin were examined. The response to serotonin declined markedly during early development and was very low at maturity. Adenylate cyclase activity in the particulate fraction from colliculi of newborn rats was significantly stimulated by serotonin. Half-maximal activation was produced with less than 1 micromolar serotonin. Tryptamine and several derivatives of serotonin produced responses which were comparable to that obtained with serotonin; 5-methoxytryptamine was uniformly the most active compound tested. Norepinephrine or dopamine produced much smaller increases in adenylate cyclase activity. Stimulation of collicular adenylate cyclase by serotonin was significantly but incompletely blocked by serotonin antagonists. In contrast, L-lysergic acid diethylamide, haloperidol, propranolol, phenoxybenzamine and morphine were ineffective as serotonin blocking agents. Of the compounds which produed a partial blockade of serotonin action, D-LSD, cyproheptadine and chlorpromazine were themselves capable of stimulating adenylate cyclase activity. These results are consistent with the existence of multiple receptors in rat brain which are capable of interacting with indoleamines. 30 references. (Author abstract modified)

217399 Cohen, Edith L.; Wurtman, Richard J. Department of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **Brain acetylcholine: increase after systemic choline administration.** Life Sciences. 16(7):1095-1102, 1975.

In a study of brain acetylcholine, administration of choline chloride i.p. to rats caused a dose dependent increase in the brain concentration of the neurotransmitter acetylcholine (ACh). This increase was maximal (22% after a 60mg/kg dose) 40 minutes after injection. These observations suggest that precursor availability may influence brain ACh synthesis, just as brain tryptophan and tyrosine levels have previously been shown to control the syntheses of brain serotonin and catecholamines. 24 references. (Author abstract modified)

217456 Chiueh, C. C.; Moore, K. E. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **Blockade of reserpine of methylphenidate-induced release of brain dopamine.** Journal of Pharmacology and Experimental Therapeutics. 193(2):559-563, 1975.

The blockage by reserpine of methylphenidate induced release of brain dopamine was examined in the cat. The cerebroventricular systems of cats were perfused by introducing artificial cerebrospinal fluid into a lateral ventricle and collecting the perfusate at the aqueduct. 3H-tyrosine was continuously added to the perfusing cerebrospinal fluid and the perfusate was analyzed for 3H-catecholamines. Intraventricular or intravenous administration of methylphenidate increased the efflux of 3H-dopamine. In cats pretreated with reserpine, this response to methylphenidate was reduced while the efflux of 3H-dopamine caused by d-amphetamine was slightly increased. These results provide direct biochemical evidence in support of the hypothesis that the central stimulant action of amphetamine and methylphenidate result from their abilities to preferentially release dopamine from newly synthesized and stored pools, respectively. (Author abstract)

217457 Freundenthal, Ralph I.; Martin, Jean. Battelle, Columbus Laboratories, 505 King Ave., Columbus, OH 43201 **Correlation of brain levels of barbiturate enantiomers with reported differences in duration of sleep.** Journal of Pharmacology and Experimental Therapeutics. 193(2):664-668, 1975.

The concentrations of R(+)-pentobarbital and S(-)-pentobarbital and R(+)-secobarbital and S(-)-secobarbital were determined in the brainstem, hypothalamus, cerebellum and cortex of mice after intravenous administration. No regional differences in enantiomer concentration or barbiturate/metabolite ratio were observed to account for the substantial potency differences reported for the enantiomeric forms of pentobarbital and secobarbital. Stereoselective differences in the rate of enantiomer metabolism and in stereochemical fit to the central nervous system receptor are discussed as possible reasons for the differences in duration of action. (Author abstract)

217462 Sayers, A. C.; Burki, H. R.; Ruch, W.; Asper, H. Research Institute Wander Ltd., P.O. Box 2747, CH-3001

Berne, Switzerland **Neuroleptic-induced hypersensitivity of striatal dopamine receptors in the rat as a model of tardive dyskinesias. Effects of clozapine, haloperidol, loxapine and chlorpromazine.** Psychopharmacologia (Berlin). 41(2):97-104, 1975.

The abilities of clozapine, haloperidol, chlorpromazine and loxapine to induce dopamine (DA) receptor hypersensitivity in rats, as measured by the apomorphine response after withdrawal of the antipsychotic drugs were examined. Haloperidol, chlorpromazine and loxapine, but not clozapine, potentiated the apomorphine response during 1-2 weeks after withdrawal. Clozapine, given prior to apomorphine, reduced the responses of the haloperidol and loxapine groups to the control level. The effects of haloperidol and clozapine were quantified in rats with unilateral striatal lesions. Biochemical investigations showed that tolerance developed to the increase in striatal homovanillic acid (HVA) after chronic treatment with haloperidol, chlorpromazine and loxapine, whereas clozapine failed to affect the HVA content, and no tolerance developed to the increase seen at 80mg/kg. Cross-tolerance to the rise in HVA was seen with haloperidol, chlorpromazine and loxapine, but chronic pretreatment with clozapine failed to affect the rise in HVA induced by a single dose of the former compounds. It is predicted that tardive dyskinesias are unlikely to develop after this drug, and that clozapine may attenuate or abolish neuroleptic induced tardive dyskinesias. 22 references. (Author abstract)

217467 Willinsky, M. D.; Loizzo, A.; Longo, V. G. Department of Surgery, University of Toronto, Toronto, Canada **EEG spectral analysis for the evaluation of the central effects of delta6-tetrahydrocannabinol in rabbits.** Psychopharmacologia (Berlin). 41(2):123-126, 1975.

The effects of delta6-tetrahydrocannabinol (THC) on the frequency spectrum of the hippocampal electroencephalogram were examined with the assistance of an electronic integrator; six rabbits bearing chronically implanted cortical and hippocampal electrodes were dosed intravenously with THC once a week. A comparison of epochs of arousal in the predrug control and postdrug period demonstrated that a dose as low 50 micrograms/kg produced a consistent, statistically significant diminution in power of the 7, 8, 9 Hz frequencies of the hippocampal EEG, with 8 Hz the most sensitive. Doses above 250 micrograms/kg produced an overall decrease in the power spectrum from 7 to 27 Hz. Spectral analysis of the EEG offers a method which is sufficiently sensitive to reveal a central effect of THC in rabbits at doses equivalent to the human threshold for psychic effects. 8 references. (Author abstract modified)

217469 Dolphin, A.; Jenner, P.; Marsden, C. D.; Pycock, C.; Tarsy, D. University Department of Neurology, Institute of Psychiatry, De Crespigny Park, London, S.E. 5, England **Pharmacological evidence for cerebral dopamine receptor blockade by metoclopramide in rodents.** Psychopharmacologia (Berlin). 41(2):133-138, 1975.

Evidence of a cerebral dopamine receptor blockade by metoclopramide was examined in rodents. Metoclopramide antagonized apomorphine induced stereotypy in rats, apomorphine reversal of reserpine reduced locomotor suppression in mice (50% inhibition produced by 17mg/kg), and apomorphine or amphetamine induced turning behavior in mice with unilateral lesions of the striatal dopaminergic nerve terminals. Metoclopramide resembles pimozide in all these respects and appeared to be a relatively potent antagonist of striatal dopamine receptors. Yet metoclopramide, in antiemetic doses, had no effect on disability in Parkinson's disease or on the therapeutic benefit of L-Dopa and L-Dopa dyskinesias. 20 references. (Author abstract)

217471 Squires, Richard F.; Lassen, Jorgen Buus. Research Laboratories, A/S Ferrosan, Sydmarken 1-5, DK-2860, Soeborg, Denmark **The inhibition of A and B forms of MAO in the production of a characteristic behavioural syndrome in rats after l-tryptophan loading.** Psychopharmacologia (Berlin). 41(2):145-151, 1975.

The effects of l-tryptophan administered to rats pretreated with selective inhibitors of the A and B forms of monoamine oxidase (MAO) were examined. Deprenyl, a selective inhibitor of MAO-B, produced only minor changes in behavior and in the concentrations of apparent 5-hydroxytryptamine (5-HT) and 5-hydroxindoleacetic acid (5-HIAA) in brain. High doses of clorgyline, a selective inhibitor of MAO-A, produced a characteristic stereotyped syndrome of hypermotility and tremor as well as an increase in apparent 5-HT and a decrease in apparent 5-HIAA in brain. Small doses of deprenyl and clorgyline in combination, but not singly, produced maximal effects on behavior as well as on the concentrations of apparent 5-HT and 5-HIAA in brain. Maximum behavior and biochemical effects were also produced when either deprenyl or clorgyline was administered 18 hrs before the other. It is concluded that the syndrome may be dependent on the formation of an N-substituted derivative of 5-HT which is at least partly deaminated by MAO-B. Alternatively, the syndrome may be dependent on a sufficiently high concentration of 5-HT in a special compartment where it is partly deaminated by MAO-B. 34 references. (Author abstract)

217472 Costall, B.; Kelley, D. M.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, Yorkshire, England **Nomifensine: a potent dopaminergic agonist of antiparkinson potential.** Psychopharmacologia (Berlin). 41(2):153-164, 1975.

In a study of a new potent dopaminergic agonist of antiparkinson potential, nomifensine was shown to be a potent stereotypic agent in the rat. Its effect was resistant to alpha-methylparatyrosine pretreatment but was abolished by combined reserpine/ampt and by haloperidol. Electrolytic lesions placed in dopamine containing areas of the extrapyramidal, mesolimbic and amygdaloid systems indicated an effect in all areas, but the globus pallidus and substantia nigra were shown to be most important for its action. The effect of nomifensine was reduced by lesions of the medial and/or dorsal raphe nuclei. A circling behavior was recorded following nomifensine administration to animals with unilateral electrolytic lesions of the substantia nigra or asymmetric lesions of the medial raphe nucleus. These effects were resistant to ampt and inhibited by haloperidol. Nomifensine reduced the intensity of harmine induced tremor. Nomifensine metabolite was shown to be a potent dopaminergic agonist with an action mainly dependent upon functioning of the extrapyramidal system and partly independent of presynaptic mechanisms. 30 references. (Author abstract modified)

217473 Ariyanayagam, A. D.; Handley, Sheila L. Pharmacological Laboratories, Department of Pharmacy, University of Aston, Birmingham, B4 7ET, England **Effect of sensory stimulation on the potency of cataleptogens.** Psychopharmacologia (Berlin). 41(2):165-167, 1975.

The effect of sensory stimulation on the potency of cataleptogens was examined in mice. Pressures of up to 100mm Hg applied to the mouse tail caused marked enhancement of the

cataleptogenic potency of morphine, haloperidol and arecoline. Visual and auditory stimuli of moderate intensity also enhanced morphine catalepsy. Thus potentiation of cataleptogens by alteration of sensory input appears to be a fairly general phenomenon. 5 references. (Author abstract)

217476 Glow, Peter H.; Russell, Alan. Department of Psychology, University of Adelaide, Aldelaide, S. A. 5001, Australia **The effects of a dexamphetamine-amylobarbitone sodium mixture on the reward value of different sensory changes.** Psychopharmacologia (Berlin). 41(2):181-185, 1975.

The effect of a dexamphetamine - amylobarbitone mixture (1:6.5by weight) on a sensory contingent bar pressing (SCBP) for different sensory changes was investigated. The aim was to examine the role of reward value of contingent change per se (nondrug) and stimulus properties in enhanced SCBP under the drug mixture. The sensory reinforcers used were light onset, light offset, and sound offset combined with the light changes contemporaneously. In the first two phases the sensory stimuli were given as continuous reinforcement and in the third phase on an FR2 schedule. The results from the first two phases were consistent with the notion that the drug mixture operates to increase the nondrug reward value of SCBP. Instead, responding under the mixture was enhanced in proportion to the level of nondrug responding, especially in Phase 1. It was concluded that properties of the sensory stimuli other than their reward value per se (nondrug) may also be related to the extent of SCBP enhancement under the drug mixture. In particular, properties of the sound offset reinforcer appear to make it more amenable to enhancement under the drug than the two light reinforcers. 8 references. (Author abstract modified)

217520 Myers, R. D.; Melchior, Christine L. Laboratory of Neuropsychology, Purdue University, West Lafayette, IN 47907 **Dietary tryptophan and the selection of ethyl alcohol in different strains of rats.** Psychopharmacologia (Berlin). 42(2):109-115, 1975.

Rats of three different strains were tested systematically for their selection of water or ethanol offered in a two choice situation. In order that preference - aversion curves could be derived, the concentrations of ethanol were increased in strength from 3 to 30% over an 11 or 12 day test sequence. L-tryptophan was added to the rat's diet in 1% or 3% mixtures for a predetermined interval beginning before or during a test for ethanol preferance. Given to female hooded rats of the Royal Victoria strain, excess tryptophan elevated the ethanol preference threshold and significantly increased ethanol intake according to the dose administered. However, in male hooded rats of the Long-Evans strain, tryptophan augmented only slightly the selection of ethanol. Male Sprague-Dawley rats, an albino strain, were unaffected by the addition of this essential amino acid to their diet. Although tryptophan may exert its effect on ethanol intake through an alteration in the metabolism of cerebral serotonin, such an effect seems to be dependent upon the strain of rat tested. 34 references. (Author abstract)

217522 Holloway, Joan A. Department of Psychiatry, University of Oklahoma Health Sciences Center, 800 N.E. 13th, P. O. Box 26901, Oklahoma City, OK 73190 **Norepinephrine and serotonin: specificity of release with rewarding electrical stimulation of the brain.** Psychopharmacologia (Berlin). 42(2):127-134, 1975.

Using a push - pull cannula method, the amygdala of rats was perfused to examine the release of labeled norepinephrine (NE) and labeled serotonin (5-HT) during electrical stimulation of the brain (ESB) determined by prior behavioral testing to be rewarding or nonrewarding. Simple sensory stimulation was used during perfusion to examine further the degree of specificity of release of these amines. Highly rewarding ESB, but not the sensory stimulation, was accompanied by release of both NE and 5-HT. Varying current intensity had significant effects on the amount of these amines released. Furthermore, nonrewarding ESB was accompanied by inhibition of release of NE and 5-HT and a control substance, urea, was not significantly released during rewarding ESB. The results are discussed as implicating both noradrenergic and serotonergic mechanisms in the mediation of reinforcement. 26 references. (Author abstract)

217527 Nahorski, S. R. Section of Pharmacology, Academic Division of Medicine, The University, Sheffield S10 2TN, England **Behavioural supersensitivity to apomorphine following cerebral dopaminergic denervation by 6-hydroxydopamine.** Psychopharmacologia (Berlin). 42(2):159-162, 1975.

The effect of central chemical sympathectomy induced by 6-hydroxydopamine on the dose - response relationships of the stimulant behavior produced by apomorphine in mice was studied. Intraventricular injections of 6-hydroxydopamine that induce a marked and long lasting depletion of cerebral dopamine as well as noradrenaline, greatly enhanced the stimulation of locomotor activity of mice produced by the injection of apomorphine. Dose response relationships indicated that the maximal response to apomorphine was greatly increased but that there was no apparent change in the ED50 from the response in vehicle treated mice. 6-Hydroxydopamine treated mice were also considerably less susceptible to the cataleptic activity of pimozide and it is suggested that cerebral dopaminergic denervation may result in an increased number of available postsynaptic dopamine receptors. 22 references. (Author abstract)

217543 Burki, H. R.; Ruch, W.; Asper, H. Wander Research Institute, P.O. Box 2747, CH-3001 Bern, Switzerland **Effects of clozapine, thioridazine, perlapine and haloperidol on the metabolism of the biogenic amines in the brain of the rat.** Psychopharmacologia (Berlin). 41(1):27-33, 1975.

The effects of clozapine, thioridazine, perlapine and haloperidol on the metabolism of the biogenic amines in the brain of the rat have been investigated. Haloperidol, perlapine and thioridazine induce catalepsy and enhance the turnover of dopamine (DA) in the striatum, as indicated by the dose dependent increase in the DA metabolites, homovanillic acid (HVA) and 3,4-dihydroxyphenylacetic acid (DOPAC). These effects are due to blockade of dopaminergic transmission, haloperidol being far more potent than perlapine or thioridazine. Clozapine differs from these agents in that it elevates the concentration of striatal DA. The increase of the concentrations of HVA and DOPAC by clozapine is not accompanied by development of catalepsy. Therefore, clozapine seems to influence striatal DA by a mechanism other than DA receptor blockade. All four drugs enhance the turnover of noradrenaline (NA) in the brainstem. This effect is probably secondary to the blockage of NA receptors. Clozapine increases the concentration of 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid in the brain. This effect was not seen with the other drugs. Perlapine seems to enhance the turnover of 5-HT, whereas haloperidol reduced the 5-HT concentration. Thioridazine appears to have no effect on the metabolism of 5-HT. 33 references. (Author abstract modified)

217544 Mirsky, Allan F.; Tecce, Joseph J.; Harman, Nancy; Oshima, Helen. Division of Psychiatry, Boston University School of Medicine, 80 E. Concord St., MA 02118 **EEG correlates of impaired attention performance under secobarbital and chlorpromazine in the monkey.** Psychopharmacologia (Berlin). 41(1):35-41, 1975.

The effects of secobarbital and chlorpromazine upon behavior in a continuous, rapidly presented successive (go - no go) discrimination (attention) task were evaluated in six Macaca mulatta monkeys. Simultaneous monitoring of electroencephalogram (EEG) activity from epidural and subcortical electrodes permitted an evaluation of the nature of altered central nervous system events during erroneous performance (errors of omission) on this task. The computer assisted analysis of prestimulus and poststimulus EEG frequency activity (baseline crossings) suggests that the best measure of attentive behavior from the prestimulus EEG is percentage of beta 2(25-40 cps) activity. No difference could be observed between drugs or among cerebral placements in this regard. This was determined by comparing measures of EEG frequency, pooled for a given test period, with performance from the same test period. The results were interpreted in terms of the hypothesis that secobarbital produces errors by depression of the general level of activation whereas chlorpromazine acts by reducing the sensory input which is necessary for correct discrimination performance. 9 references. (Author abstract modified)

217553 Forrest, I. S.; Green, D. E.; Serra, M. T.; Soave, O. A. Biochemical Research Laboratory, VA Hospital, Palo Alto, CA 94304 **Chlorpromazine excretion in chronically dosed primates. I. Occurrence of a previously unreported class of chlorpromazine conjugates.** Psychopharmacology Communications. 1(1):51-59, 1975.

In a study of chlorpromazine excretion, 14C-labeled chlorpromazine was administered to rhesus monkeys. All unconjugated chlorpramzine metabolites were exhaustively extracted, and an alkaline hydrolysis performance. The aglycones liberated thereby were again carefully removed, and the residual aqueous fraction was subjected to an acid hydrolysis. This procedure yielded an additional group of known and unknown phenolic chlorpromazine aglycones, representing approximately one third of the radioactivity in the whole urine. Preliminary trials on urine pools of patients chronically dosed with chlorpromazine yielded essentially the same results. The structure of this new class of chlorpromazine conjugates has not yet been elucidated, nor is the ligand known at this time. A glucoside type bond may characterize this significant class of chlorpromazine conjugates. 12 references. (Author abstract modified)

217555 Baumgarten, Hans G.; Victor, Stephen J.; Lovenberg, Walter. Department of Neuroanatomy, University of Hamburg, Hamburg, Germany **A developmental study of the effects of 5,7-dihydroxytryptamine on regional tryptophan hydroxylase in rat brain.** Psychopharmacology Communications. 1(1):75-88, 1975.

The effects of 5,7-dihydroxytrypamine (5,7-DHT) on regional tryptophan hydroxylase in rat brain were examined. Trytophan hydroxylase activity rises rapidly after birth in five distinct regions of the rat central nervous system (CNS). Near adult levels of activity are recorded by 22 days old in the cell body rich regions of the brainstem and by 42 days in the terminal rich areas, hypothalamus and remaining forebrain. The intracisternal injection of 5,7-dihydroxytryptamine on day 2 after birth results in a near total depletion of tryptophan hydroxylase in all CNS regions analyzed 6 or 12 days after drug administration. Enzyme activity recovers (to 11-24% of age matched controls) between midbrain and pons medulla oblongata. The growth of 5,7-DHT treated animals is retarded between 3 and 40 days after drug administration. 23 references. (Author abstract)

217575 Van Zwieten, P. A. Department of Pharmacotherapy, Plantage Muidergracht 24, Amsterdam-C, The Netherlands **Interaction between centrally acting hypotensive drugs and tricyclic antidepressants.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 214(1):12-30, 1975.

The hypotensive action of clonidine and alpha-methyl-DOPA, which is antagnoized by desipramine, was investigated in chloralose anesthetized cats. The central hypotensive action of clonidine was antagonized by desipramine, imipramine, amitriptyline, protriptyline and mianserine. For the inhibition of the hypotensive action of clonidine by protriptyline, a parallel shift of the dose response curve was obtained, indicating the possibility of a competitive antagonism. The central hypotensive action of alpha-methyl-DOPA was antagnozied by desipramine and imipramine and that of amphetamine by imipramine. It is suggested that the antagonism reflects a general interaction between centrally acting hypotensive drugs and tricyclic antidepressants. The alpha-sympatholytic properties of the tricyclic antidepressants probably give rise to a blockade of the central alpha-adrenoreceptors, stimulated by clonidine, noradrenaline (via amphetamine) and alpha-methyl-noradrenaline. 39 references. (Author abstract modified)

217638 Pentreath, V. W. Wellcome Laboratories of Pharmacology, Univesity of St. Andrews, St. Andrews, Fife, Scotland **Effects of 5,7-dihydroxytryptamine on trasmission at serotoninergic synapese.** Journal of Pharmacy and Pharmacology (London). 27(4):293, 1975.

To test the specificity of the effect of 5,7-dihydroxtryptamine (DHT) on the excitatory postsynaptic potential (EPSP) elicited by the 5-HT neuron, different nerve trunks were stimulated to produce large epsps from a different source. Such epsps are thought to be cholinergic. They were not altered in amplitude by 5,7-dihydroxytryptamine. Furthermore, no appreciable reduction in membrane resistance due to 5,7-dihydroxytryptamine produced a relatively specific blockade of serotoninergic transmission by blocking 5-HT receptors. (Author abstract modified)

217649 Zakusov, V. V.; Ostrovskaya, R. U.; Markovitch, V. V.; Molodavkin, G. M.; Bulayev, V. M. Institute of Pharmacology, Academy of Medical Sciences, Moscow, U.S.S.R. **Electrophysiological evidence for an inhibitory action of diazepam upon cat brain cortex.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 214(2):188-205, 1975.

In an electrophysiological study of diazepam upon cat brain cortex, diazepam was shown to increase postexcitatory inhibition within the brain cortex, as revealed by its influence upon the recovery cycles both of intracortical and primary responses. The specific interrelationship between diazepam and some drugs affecting brain gamma-aminobutyric acid (GABA) levels suggests the possibility of a GABA mediated mechanism in the diazepam effect. The sensitivity of the brain cortex to diazepam is not lower than that of the amygdala and is significantly higher than that of the hippocampus. 54 references. (Author abstract)

217650 Winter, J. C. Department of Pharmacology and Therapeutics, School of Medicine, SUNY, Buffalo, NY 14214

Blockade of the stimulus properties of mescaline by a serotonin antagonist. Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 214(2):250-253, 1975.

The ability of cinanserin, a serotonin antagonist, to block the stimulus properties of mescaline in the rat was examined. After a reliable discrimination was established between the effects following the injection of mescaline and those following administration of saline, subjects were pretreated with cinanserin HCl and then treated with mescaline. Such pretreatment was found to block discrimination, i.e.,the response rate following the administration of mescaline plus cinanserin was appropriate for the saline condition. 22 references. (Author abstract modified)

217651 Turker, R. K.; Kaymakcalan, S.; Ercan, Z. S. Department of Pharmacology, Faculty of Medicine, University of Ankara, Ankara, Turkey **Antihistaminic action of (-)-trans-delta-9-tetrahydrocannabinol.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 214(2):254-262, 1975.

The antihistaminic action of (-)-trans-delta9-tetrahydrocannabinol (THC) was examined in isolated perfused guinea pig lung and rabbit kidney. This antagonism was a competitive one at the concentrations used and interacted with histamine at H1-receptors. THC also antagonized the effect of acetylcholine, PGE2, angiotensin II and histamine in the isolated continuously superfused guinea pig ileum by a noncompetitive manner. The antagonism between THC and histamine on the isolated superfused rabbit aortic strips was found to be highly specific, since 100% relaxation was obtained when the muscle contracted by histamine but not by the equipotent doses of angiotensin II and noradrenaline. THC caused a significant increase in survival time of guinea pigs when the animals were exposed to histamine aerosol. These results indicate a specific antagonism of THC against histamine in the preparations used in this investigation. 12 references. (Author abstract)

217653 Engstrom, R. G.; Kelly, L. A.; Gogerty, J. H. Biochemistry Section, Sandoz Pharmaceuticals, East Hanover, NJ 07936 **The effects of 5-hydroxy-5-(4'-chlorophenyl)-2, 3-dihydro-5H-imidazo (2, 1-a) isoindole (Mazindol, SaH 42-548) on the metabolism of brain norepinephrine.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 214(2):308-321, 1975.

The effects of Mazindol, 5-hydroxy5-(4'-chlorophenyl)-2 3-dihydro-5H-imidazo-(2, 1-a) isoindole on neuronal uptake and/or release of norepinephrine were studied. Mazindol, when given before cerebral intraventricular injection of 3H-norepinephrine, rapidly reduced the accumulation of H-norepinephrine by a mechanism that increases 3H-normetanephrine synthesis via catechol-O-methyltransferase and provided no significant effect on deamination of the catecholamine. Studies designed to measure norepinephrine release showed that Mazindol (in contrast to d-amphetamine) did not cause release of 3H-norepinephrine from neuronal stores. Furthermore, Mazindol did not inhibit norepinephrine synthesis, whereas d-amphetamine did. The effect of d-amphetamine on norepinephrine release and synthesis may be more important than effects on uptake of this catecholamine. In contrast, Mazindol appears to produce its primary effect on norepinephrine metabolism by inhibition of neuronal uptake mechanism. 19 references. (Author abstract modified)

217654 Geber, W. F.; Lefkowitz, S. S.; Hung, C. Y. Department of Pharmacology, Medical College of Georgia, Augusta, GA 30902 **Effect of morphine, hydromophone, methadone, mescaline, trypan blue, vitamin A, sodium salicylate and caffeine on the serum interferon level in response to viral infection.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 214(2):322-327, 1975.

The ability of morphine, hydromorphone, methadone, mescaline, trypan blue, vitamin A, sodium salicylate and caffeine to alter the circulating serum level of interferon was investigated in mice. Sodium salicylate and caffeine increased the serum level of interferon; however, the interferon increase produced by sodium salicylate was dose dependent, i.e. low doses increased interferon titers, high doses decreased the titers. All other compounds decreased the circulating level of interferon. These results suggest that compounds of varied structure and biological activity, and possessing teratogenic potential, are capable of depressing the circulating level of interferon. Some of these antiinterferon compounds, i.e. morphine, hydromorphone, methadone, depressed interferon levels at all doses whereas sodium salicylate decreased the interferon level only at relatively high dose levels. 28 references. (Author abstract)

217655 Bourgoin, S.; Ternaux, J. P.; Boireau, A.; Hery, F.; Hamon, M. Groupe NB INSERM U 114, College de France, 11, place Marcelin Berthelot, F-75005 Paris, France **Effects of halothane and nitrous oxide anesthesia on 5-HT turn-over in the rat brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 288(2/3):109-121, 1975.

The effects of anesthesia with halothane and nitrous oxide on the turnover of 5-hydroxytryptamine (5-HT) in the rat brain were analyzed. The rate of 5-HT synthesis was estimated on the basis of 5-hydroxyindoleacetic acid accumulation following 5-hydroxytryptophen (5-HTP) decarboxylase inhibition. Inhalation anesthetics reduced the rate of 5-HT synthesis in the whole brain, this effect being particularly marked in the forebrain. In addition, the reduction of the rate of 5-HT synthesis was still detected after a large tryptophan loading indicating that halothane and nitrous oxide anesthesia reduced the activity of tryptophan hydroxylase in vivo. The utilization of 5-HT was also delayed during anesthesia since the rate of 5-HT disappearance following the inhibition of its synthesis at the decarboxylation step was decreased in the whole brain. In spite of this reduced turnover of 5-HT in the brain of rats exposed to inhalation anesthetics, the 5-hydroxyindoleacetic acid levels were permanently elevated. This was the result of a partial inhibition of the active elimination of the acidic metabolite from the brain during this kind of anesthesia. 15 references. (Author abstract)

217657 Barth, N.; Manns, M.; Muscholl, E. Pharmakologisches Institut der Universitat, D-6500 Mainz, Obere Zahlbacher Strasse 67, Germany **Arrhythmias and inhibition of noradrenaline uptake caused by tricyclic antidepressants and chlorpromazine on the isolated perfused rabbit heart.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 288(2/3):215-231, 1975.

Arrhythmias and inhibition of noradrenaline and chlorpromazine uptake caused by tricyclic antidepressants were examined on the isolated perfused rat heart. Infusions of noradrenaline evoked ventricular arrhythmias in hearts perfused with amitriptyline, chlorpromazine, desipramine, dibenzepine, doxepin, imipramine, noxiptiline and opipramole. The incidence of arrhythmias increased with the concentration of noradrenaline applied and the dose of tricyclic drug administered. Whenever arrhythmias had started they continued as long as noradrenaline was infused. Noradrenaline failed to produce arrhythmias in hearts not exposed to drugs and after

iprindole or cocaine. Propranolol inhibited the incidence of arrhythmias after doxepin plus noradrenaline. Neuronal uptake of exogenous noradrenaline in the rabbit heart was inhibited by the tricyclic drugs in the following order of declining potency: doxepin, noxiptiline, amitriptyline, desipramine, chlorpromazine, imipramine, dibenzepine, opipramole and iprindole. 32 references. (Author abstract modified)

217658 Guyenet, P. G.; Beaujouan, J. C.; Glowinski, J. Groupe NB (INSERM U. 114), College de France, 11, Place Marcelin Berthelot, F-75005, Paris, France **Ontogenesis of neostriatal cholinergic neurones in the rat and development of their sensitivity to neuroleptic drugs.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 288(2/3):329-334, 1975.

Simultaneous determinations of the striatal contents in acetylcholine (ACh), choline acetyltransferase (ChAc) and acetylcholinesterase (AChE) were made in neonate rats from day 4 to day 16 after birth. While, during this period, ChAc and AChE increased 14 and 5 fold, respectively, the change of ACh levels was smaller and more gradual. ACh levels were unaltered following the injection of thioproperazine (5mg/kg) until day 8, then within 6 days the cholinergic neurons developed a full sensitivity to this drug. The sensitivity to haloperidol (4mg/kg), pimozide (4mg/kg) and to the dopamine receptor stimulating drug apomorphine (10mg/kg) appeared along with that to thioproperazine. These data confirm that rat striatal cholinergic neurons are immature at birth. They suggest, in addition, that the development of dopamine receptors occurs prior to the appearance of functional cholinergic synapses or concomitant with this event. 19 references. (Author abstract)

217659 Daniell, Herman B. Department of Basic and Clinical Pharmacology, Medical University of South Carolina, Charleston, SC 29401 **Cardiovascular effects of diazepam and chlordiazepoxide.** European Journal of Pharmacology (Amsterdam). 32(1):58-65, 1975.

The cardiovascular effects of diazepam and chlordiazepoxide were studied. In open chest dog preparations i.v. administration of diazepam and chlordiazepoxide caused increases in coronary blood flow and cardiac output while reducing blood pressure, heartrate, and myocardial contractile force. The decrease in force was independent of the alteration in coronary flow. Arterial - coronary sinus oxygen difference narrowed and myocardial oxygen consumption decreased. These data show that both diazepam and chlordiazepoxide exert an oxygen conserving action along with an increase in myocardial oxygen delivery and suggest that these drugs may be of benefit to the patient with coronary insufficiency by a direct effect on the cardiovascular system as well as through central nervous system mediated antianxiety effects. 19 references. (Author abstract)

217661 Halaris, Angelos E.; Freedman, Daniel X. Department of Psychiatry, University of Chicago, Chicago, IL 60637 **Loss of body weight as a predictor of reserpine induced amine depletion.** European Journal of Pharmacology (Amsterdam). 32(1):93-101, 1975.

Loss of body weight was proved to be a convenient and reliable way to predict the degree of reserpine induced amine depletion after i.p. injections of reserpine and it thus helps reduce variability. One group lost less than 5% of their body weight, showed absence of physiological and behavioral effects, a moderate depletion and a moderate 5-hydroxyindoleacetic (5HIAA) acid increase. These animals were called partially reserpinized. Another group always lost 5% or more of body weight, exhibited the reserpine syndrome as well as a larger extent of 5-hydroxytryptamine (5-HT) depletion and 5-HIAA increase. This group comprised reserpinized rats. There were significant correlations between the percent weight loss and the degree of 5-HT depletion and 5-HIAA increase in the group of partially reserpinized animals. 20 references. (Author abstract modified)

217662 Frazier, Donald T.; Murayama, Koichi; Abbott, N. Joan; Narahashi, Toshio. Department of Physiology and Biophysics, Medical Center, University of Kentucky, Lexington, KY 40506 **Comparison of the action of different barbiturates on squid axon membranes.** European Journal of Pharmacology (Amsterdam). 32(1):102-107, 1975.

Experiments utilizing squid giant axons were carried out to determine if the duration of anesthesia obtained from phenobarbital, pentobarbital and hexobarbital can be explained by events related to their action at the nerve membrane level. For comparison, the barbiturates were perfused both outside and inside the squid axon at concentrations which produced an approximately equivalent depression of the maximum rate of rise of the action potential. The time to 50% maximum block and the time to 50% maximum recovery following washing were compared for all three drugs. All three barbiturates were more potent from inside the squid axon than from the outside. This finding coupled with the fact that the time course of the drug effects was much shorter when applied inside as compared to outside suggests an internal site of action. 12 references. (Author abstract modified)

217663 Lassen, Jorgen Buus; Peterson, Erling; Kjellberg, Bengt; Olsson, Sven O. Research Laboratories of Ferrosan, Copenhagen, Denmark **Comparative studies of a new 5-HT uptake inhibitor and some tricyclic thymoleptics.** European Journal of Pharmacology (Amsterdam). 32(1):108-115, 1975.

The new 5-hydroxytryptamine (5-HT) uptake inhibitor, FG 4963, and some tricyclic thymoleptics which antagonized p-chloroamphetamine (PCA) induced hypermotility in rats was studied. FG 4963 was active in about the same s.c. and p.o. doses as chlorimipramine. FG 4963, imipramine and chlorimipramine potentiated hypermotility induced in mice by the 5HT precursor, 5-hydroxytryptophan, FG 4963 being slightly more active than chlorimipramine. In contrast to the tricyclic thymoleptics FG 4963 did not potentiate the heartrate increasing effect of noradrenaline (NA) in pithed rats. The peripheral anticholinergic effect of FG 4963 and of desipramine was almost identical while the other imipramine derivatives were more active. All tricyclic thymoleptics were strong peripheral antihistaminics, but FT 4963 was almost devoid of this action. Acute tests for electrocardiogram changes in guinea-pigs and toxicity in mice and rats showed that FG 4963 and chlorimipramine were less toxic than imipramine and amitriptyline. FG 4963 is presumably a selective 5HT uptake inhibitor producing much less potentiation of peripheral sympathetic mechanisms than do the tricyclic antidepressants. 40 references. (Author abstract)

217664 Dominic, Jerome A.; Sinha, Arabinda K.; Barchas, Jack D. Department of Pharmacology, University of Kentucky, Lexington, KY 40506 **Effect of benzodiazepine compounds on brain amine metabolism.** European Journal of Pharmacology. 32(1):124-127, 1975.

The effect of benzodiazepine compounds on brain amine metabolism was examined in mice. In mice, chlordiazepoxide, diazepam and flurazepam reduced 5-hydroxytryptamine (5-HT) synthesis and metabolism in the teldiencephalon following an

i.v. injection of 3H-tryptophan. Only diazepam produced a significant effect in the brainstem. The steady state level of brain 5-HT or of tryptophan was not altered by any of the drugs. Chlordiazepoxide and diazepam, but not flurazepam, decreased the rate of norepinephrine loss from the brain following inhibition of synthesis with alpha-methyl-tyrosine. 12 references. (Author abstract)

217665 Warsh, Jerry J.; Stancer, Harvey C. Department of Neurochemistry, Clarke Institute of Psychiatry, University of Toronto, 250 College Street, Toronto, Canada M5T IR8 **The origin of blood 5-hydroxyindoleacetic (5HIAA) acid following L-hydrazino-alpha-methyldopa (MK-486).** European Journal of Pharmacology (Amsterdam). 32(1):128-132, 1975.

Blood 5-hydroxyindoleacetic (5HIAA) acid (5-HIAA) levels derived from exogenous labelled D,L-5-hydroxytryptophan (5-HTP) were investigated in normal, sham operated and nephrectomized rats pretreated with L-hydrazino-alpha-methyldopa (MK-486) and probenecid (200mg/kg i.p.). Blood 5-HIAA levels decreased in nephrectomized rats following probenecid. Peripheral decarboxylase inhibition by MK-486 was enhanced by both probenecid and nephrectomy. Increased penetration of 5-HTP into brain occurred following probenecid. The results indicate that following MK-486 about 20% of the blood 5-HIAA derived from 5-HTP in rats originates in the central nervous system. 14 references. (Author abstract)

217669 Baker, Walter W.; Zivanovic, Dragan; Malseed, Roger T. Division of Neuropharmacology, Eastern Pennsylvania Psychiatric Institute, Philadelphia, PA **Contrasting local effects of MAO inhibitors on caudate tremor activities.** European Journal of Pharmacology (Amsterdam). 31(1):17-22, 1975.

Contrasting local effects of monoamine oxidase (MAO) inhibitors on caudate tremor activities are reported. Hindlimb tremor was produced in chronic cats by intracaudate microinjection of the MAO inhibitors tranylcypromine and harmaline throughout a range of doses. Pargyline, however, was nontremorgenic within the same range, suggesting that interference with MAO is not sufficient in itself to elicit tremor. Tranylcypromine tremors differed from those of harmaline by exhibiting a slower onset, longer duration and susceptibility to antagonism by hemicholinium. In contrast, ongoing cholinergic tremors following intracaudate physostigmine were variably suppressed by all three MAO inhibitors at comparable dose levels; pargyline produced the most complete suppression. These results indicate that MAO inhibitors can modify tremor activities in a differential manner dependent both on the functional state of the caudate nucleus and on the ability of certain MAO inhibitors to exert other local actions. 22 references. (Author abstract)

217672 Siemens, Albert J.; De Nie, L. Cornelius; Kalant, Harold; Khanna, Jatinder M. Research Institute on Alcoholism, 1021 Main St., Buffalo, NY 14203 **Effects of various psychoactive drugs on the metabolism of delta1-tetrahydrocannabinol by rats in vitro and in vivo.** European Journal of Pharmacology (Amsterdam). 31(1):136-147, 1975.

Metabolism of 14C-tetrahydrocannabinol (THC) by rat liver microsomal preparations in vitro was studied in the absence and presence of other psychoactive drugs. Disappearance of THC, and changes in metabolite patterns as shown by thin layer chromatography, were studied. SKF 525-A, pentobarbital, phenobarbital and amphetamine all produced an apparently noncompetitive inhibition of THC metabolism. The inhibition produced by meprobamate was at least partly competitive. Morphine and mescaline had no evident effect. SKF 525-A and the barbiturates markedly decreased the concentrations of all the major THC metabolites found in the incubation media. In contrast, none of the drugs tested in vivo, with the exception of SKF 525-A, had any effect on the biliary 14C-excretion or metabolite pattern, or on final tissue levels of 14C, when administered in doses comparable to those used for studies of interaction with THC in vivo. SKF 525-A. 29 references. (Author abstract modified)

217673 Ten Ham, Martijn; Loskota, William J.; Lomax, Peter. National Institute of Public Health, Department of Pharmacology, P.O. Box 1, Bilthoven, The Netherlands **Acute and chronic effects of delta9-tetrahydrocannbinol on seizures in the gerbil.** European Journal of Pharmacology (Amsterdam). 31(1):148-152, 1975.

The acute and chronic effects of delta9-tetrahydrocannabinol (THC) on seizures in the gerbil were examined. THC was injected daily for 6 days into gerbils from our breeding colony that exhibit spontaneous epileptiform seizures. At a dose of 20mg/kg no effect was seen on the latency, duration or severity of the seizures induced after 1 and 6 days of treatment. THC (50mg/kg) completely abolished the seizures after a single injection but tolerance developed to this effect so that no protection was afforded after 6 daily doses. Severe toxic signs were evident at the higher dose level with marked depression of spontaneous motor activity. The toxic effects increased progressively with chronic treatment and half the animals failed to survive. 16 references. (Author abstract)

217674 Hollunger, Gunnar; Persson, Sven-Ake. Department of Pharmacology, University of Umea, S-901 87, Vnea, Sweden **The effect of LSD and 2-bromo LSD on the DOPA accumulation after central and peripheral decarboxylase inhibition.** European Journal of Pharmacology (Amsterdam). 31(1):156-158, 1975.

The effect of lysergic acid diethylamide (LSD) and 2-bromo LSD (BOL) on the DOPA accumulation after central and peripheral decarboxylase inhibition was studied. LSD and BOL were found to be equally potent in increasing the rat brain DOPA accumulation after decarboxylase inhibition. However, at the doses selected, the DOPA levels after haloperidol and apomorphine were increased by LSD but not by BOL. It is suggested that this difference is due to LSD's activating effect on central serotoninergic receptors. 11 references. (Author abstract)

217676 Rebec, G. V.; Groves, P. M. Department of Psychology, University of Colorado, Boulder, CO 80302 **Apparent feedback from the caudate nucleus to the substantia nigra following amphetamine administration.** Neuropharmacology (Oxford). 14(4):275-282, 1975.

Spontaneous neuronal activity in the caudate nucleus, substantia nigra and mesencephalic reticular formation recorded following intraperitoneal injection of (+)-amphetamine sulfate. In the caudate nucleus (+)-amphetamine produced a brief potentiation of neuronal activity that was followed by a prolonged depression, lasting in some cases longer than 100 min. A similar response pattern was observed for neurons in the pars compacta of the substantia nigra following amphetamine administration, although the potentiation of activity was somewhat less pronounced and the duration of depression was more variable. Neurons in the pars reticulata of the substantia nigra displayed only a prolonged increase in activity after drug injection, as did neurons in the mesencephalic reticular formation. The results are discussed in terms of a possible feedback

control of dopaminergic transmission in the nigrostriatal pathway. 29 references. (Author abstract)

217677 Nahorski, S. R.; Rogers, K. J. Section of Pharmacology, Academic Division of Medicine, The University, Sheffield S10 2TN, England **The role of catecolamines in the action of amphetamine and L-dopa on cerebral energy metabolism.** Neuropharmacology (Oxford). 14(4):283-290, 1975.

The role of dopamine and noradrenaline underlying the neurochemical effects of amphetamine in the rat were examined by means of receptor blocking drugs and 6-hydroxydopamine. The acute administration of (+)-ampetamine sulfate to rats, induced a typical stimulant behavioral syndrome that was accompanied by depletion of cerebral glycogen and an elevation of lactate and malate. Pretreatment of rats with pimozide abolished the behavioral stimulation and the increase in malate but did not influence the fall in glycogen or increase in lactate induced by amphetamine. Conversely, prior administration of propranolol attenuated the amphetamine induced changes in glycogen and lactate but neither prevented the hyperactivity nor the increase in cerebral malate. Cerebral injection of 6-hydroxydopamine, completely abolished the behavioral stimulation and cerebral metabolite changes induced by amphetamine. The administration of amphetamine to rats that had been chronically treated with the stimulant did not induce the characteristic rapid cerebral glycogenolysis but still caused behavioral stimulation and an elevation of cerebral malate. It is suggested that amphetamine may influence the release of dopamine which then acts at appropriate neuronal receptors, whereas released noradrenaline may interact with a beta-adrenoceptor on glia and there promote the breakdown of glycogen. 46 references. (Author abstract modified)

217685 Stadler, H.; Ciria, M. Gadea; Bartholini, G. Department of Experimental Medicine, F. Hoffmann-La Roche & Co. Ltd., CH-4002, Basel, Switzerland **"In vivo" release of endogenous neurotransmitters in cat limbic regions: effect of chlorpromazine and of electrical stimulation.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 288(1):1-6, 1975.

The effect of chlorpromazine on the spontaneous release of endogenous dopamine (DA), noradrenaline (NA) and acetylcholine (ACh) within limbic areas perfused by means of the push - pull cannula was investigated in the gallamine immobilized cat. Chlorpromazine increased the liberation of DA and NA in the nucleus accumbens septi, indicating blockade of the amine receptors. However, the drug did not change the output of ACh from this nucleus nor from ventral and dorsal hippocampal formations which receive a cholinergic input from the septum as indicated by several published findings and by the increased liberation of ACh after electrical stimulation of the homolateral nucleus medialis septi. These results seem to exclude that cholinergic neurons of some limbic areas mediate the effect of the blockade of DA (and of NA) receptors which is possibly involved in the antipsychotic action of neuroleptic drugs. 23 references. (Author abstract)

217687 Velley, L.; Blanc, G.; Tassin, J. P.; Thierry, A. M.; Glowinski, J. Laboratoire de Psychophysiologie, Complexe Scientifique de Cezaux, 24, avenue de Landais, F-63170-Aubiere, France **Inhibition of striatal dopamine synthesis in rats injected chronically with neuroleptics in their early life.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 288(1):97-102, 1975.

The inhibition of striatal dopamine synthesis was examined in rats injected chronically with neuroleptics in their early life. 3H-Dopamine synthesis from L-3,5-3H-tyrosine was reduced in striatal slices of 40-day-old rats treated during their early life with neuroleptics. Animals were first injected intrautero with thioproperazine or with the palmitic ester of pipotiazine; the thioproperazine treated rats were then injected every day from day 1 to day 37; the animals injected with the long-acting neuroleptic were injected once more with the drug on day 15 after birth. 20 references. (Author abstract)

217688 Pugsley, T. A.; Lippmann, W. Biochemical Pharmacology Department, Ayerst Research Laboratories, Montreal, Quebec, Canada **Effect of butriptyline on the brain uptake mechanisms for noradrenaline and 5-hydroxytryptamine.** Journal of Pharmacy and Pharmacology (London). 26(10):778-782, 1974.

In a study of brain uptake mechanisms, butriptyline, a tricyclic compound, in contrast to the tricyclic desipramine did not alter the accumulation or metabolism in areas of the rat brain of intraventricularly injected (3H)noradrenaline. It did not appreciably inhibit the displacement of 5-hydroxytryptamine (5-HT) by alpha-ethyl-3-hydroxy-4-methyl phenethylamine in comparison with the tricyclic chlorimipramine. Butriptyline potentiated central 5-hydroxytryptophan (5-HTP) effects only slightly whereas chlorimipramine displayed a strong potentiation. It is concluded that butriptyline differs significantly from desipramine, as no inhibitory effect on brain noradrenaline uptake was found, and from chlorimipramine, as only a weak inhibitory activity on brain 5-HT uptake was observed. 21 references. (Author abstract)

217690 Sever, Peter S.; Caldwell, John; Williams, R. Tecwyn. Department of Biochemistry, St. Mary's Hospital Medical School, London, W2 1PG, England **Evidence against the involvement of false neurotransmitters in tolerance to amphetamine-induced hyperthermia in the rat.** Journal of Pharmacy and Pharmacology (London). 26(10):823-826, 1974.

Evidence against the involvement of false neurotransmitters in tolerance to amphetamine induced hyperthermia in the rat is presented. p-Hydroxyamphetamine, norephedrine and p-hydroxynorephedrine only exert a protecting effect in the males, since the temperature rise after the amphetamine challenge in drug pretreated females is the same as in saline controls. The reduction in the hyperthermic response is statistically significant in the males for all three agents. The mean maximum rise in temperature after amphetamine is considerably reduced in p-hydroxyamphetamine pretreated male rats and in saline controls, but there is no significant difference between the two values in female rats similarly pretreated. The maximum temperature rise after amphetamine in p-hydroxyamphetamine pretreated male rats is significantly less than in pretreated females. 8 references.

217691 Caldwell, John; Sever, Peter S.; Trelinski, Marek. Department of Biochemistry, St. Mary's Hospital Medical School, London, W1 2PG, England **On the mechanism of the hyperthermia induced by amphetamine in the rat.** Journal of Pharmacy and Pharmacology (London). 26(10):821-823, 1974.

The mechanism of amphetamine induced hyperthermia in both male and female rats was examined to determine whether sex differences in this mechanism underlie the observed sex difference in p-hydroxynorephedrine protection. Only those pretreatments which deplete noradrenaline reduced the amphetamine hyperthermia. Ganglion blockade was ineffective suggesting that transmission through the autonomic nervous system is not involved in amphetamine hyperthermia. Similarly, the lack of effect seen with p-chloroamphetamine

would appear to indicate that 5-hydroxytryptamine in the central nervous system is not involved in the hyperthermic response to amphetamine. None of these pretreatments affect the baseline temperatures of test and control groups immediately before challenge. However, both inhibition of catecholamine synthesis and peripheral sympathectomy abolish the hyperthermic response, without affecting the basal temperature of the rats. When the peripheral sympathectomy was restricted to dopaminergic neurons, the hyperthermia was unaffected. This would appear to suggest that intact peripheral noradrenergic neurons are a prerequisite for the hyperthermic action of amphetamine. It thus appears that the mechanism of the hyperthermia induced by amphetamine in the rat is different from other species, in that it is apparently peripheral while in the mouse and rabbit it appears to be a central effect. 12 references.

217692 Lundborg, P.; Roos, B. -E. Department of Pharmacology, University of Goteborg, Fack, S-400 33 Goteborg 33, Sweden **Increased concentration of homovanillic acid in the brains of infant rabbits after administration of haloperidol to their nursing mothers.** Journal of Pharmacy and Pharmacology (London). 26(10):816-818, 1974.

An increase in brain homovanillic acid (HVA) levels of nursing rabbit infants in response to haloperidol administration to their mothers was used to test for the uptake of the drug into the mothers milk and oral intake by the infants. When haloperidol had been administered via the drinking water over 24 h, the brain HVA content of the nursing mothers increased. After treatment of the nursing mothers for 72 h before death, the brain concentrations of HVA were similarly increased in the brains of both mother and infant. The increase in HVA content after oral haloperidol was less pronounced in the infants' brain than in their mother's brain. There did not seem to be any cumulative effect of the drug since no difference was observed between the 72 and 24 h treatment. In conclusion, administration of haloperidol to nursing rabbit mothers causes an increased HVA content in the brains of both the mothers and their nursing infants, indicating that significant amounts of the drug or an active metabolite can pass into the milk and reach the nursing infants. 6 references.

217693 Buczko, W.; De Gaetano, G.; Garattini, S. Department of Pharmacology, Medical School, Bialystok, Poland **Influence of some tricyclic antidepressive drugs on the uptake of 5-hydroxytryptamine by rat blood platelets.** Journal of Pharmacy and Pharmacology (London). 26(10):814-815, 1974.

The influence of some tricyclic antidepressive drugs on the uptake of 5-hydroxytryptamine (5-HT) by rat blood platelets was examined. Chlorimipramine was the most potent inhibitor, followed by imipramine, desmethylchlorimipramine and amitriptyline; all these drugs inhibited 5-HT uptake by more than 50%; in contrast, nortriptyline, doxepine, desipramine and desmethyldoxepine inhibited the uptake of 14C-5-HT by less than 50%. For each drug, the tertiary amine appeared to be more active than the corresponding metabolite (secondary amine). The trans doxepine compound proved to be at least as active as the mixture and the cis compound was almost devoid of inhibitory activity. The present results indicate that rat platelets would be useful as a model for evaluating the rank order of the inhibitory potency of tricyclic antidepressive drugs on 14C-5-HT uptake mechanisms. 11 references.

217695 McMahon, E. M.; Feldman, J. M.; Schanberg, S. M. Department of Psychiatry, University of Washington School of Medicine, Seattle, WA 98195 **Further studies of methamphetamine-induced insulin release.** Toxicology and Applied Pharmacology. 32(1):62-72, 1975.

Factors that modify methamphetamine induced insulin secretion were studied in the mouse. While methamphetamine stimulates insulin secretion in intact rats and mice, it stimulates insulin secretion in vitro only from mouse pancreas. Related drugs such as d-amphetamine, methylphenidate, and tranylcypromine also stimulate insulin secretion in intact rats. Methamphetamine induced secretion is not altered by alpha-receptor antagonists or ganglionic blocking agents, but is reduced by beta-receptor antagonists. Insulin secretion in response to methamphetamine is significantly increased in the hyperthyroid state and decreased in the hypothyroid state. Chronic methamphetamine administration results in a reduction in the insulin secreted in response to this agent. 26 references. (Author abstract)

217696 Fuller, Ray W.; Snoddy, Harold D. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Inhibition of serotonin uptake and the toxic interaction between meperidine and monoamine oxidase inhibitors.** Toxicology and Applied Pharmacology. 32(1):129-134, 1975.

The possibility that inhibition of serotonin uptake by meperidine was the basis for the greater toxicity of the drug in animals treated with monoamine oxidase inhibitors was investigated by comparing meperidine to a new potent inhibitor of serotonin uptake, Lilly 110140(3-(p-trifluoromethylphenoxy-)-N-methyl-3-phenylpropylamine hydrochloride). The blockade of 4-chloroamphetamine induced depletion of brain serotonin was used as a measure of inhibition of uptake into serotoninergic neurons. With meperidine, the doses required to inhibit that uptake were approximately equal to doses that were lethal in tranylcypromine pretreated mice. Lilly 110140, on the other hand, inhibited uptake at doses less than 1/100 of those that were toxic in tranylcypromine pretreated mice. These findings show that inhibition of uptake into serotoninergic neurons does not in itself lead to toxic interactions with monoamine oxidase inhibitors. 21 references. (Author abstract)

217762 Maser, Jack D.; Gallup, Gordon G., Jr.; Hicks, Lou E. Clinical Research Branch, National Institute of Mental Health, 5600 Fishers Lane, Rockville, MD 20852 **Tonic immobility in chickens: possible involvement of monoamines.** Journal of Comparative & Physiological Psychology. 89(4):319-328, 1975.

Certain drugs thought to affect serotonergic centers in the midbrain and pons were given to chickens in four experiments designed to implicate monoaminergic neurons in tonic immobility (TI). Commpounds that enhanced the duration of TI were d-lysergic acid diethylamide (d-LSD), the diethylamide of 2-bromo-d-lysergic acid (BOL-148), pargyline, and iproniazid; compounds that had no effect were 5-hydroxytryptophan, para-chlorophenylalanine (p-CPA), and atropine. Injections of serotonin depressed response duration. A suggestive parallel was noted between the results and previous work which reported drug induced suppression of raphe electrical activity. The data appear to implicate monoamines, especially serotonin, in the mediation of behavioral activation and suppression. 49 references. (Author abstract modified)

217793 Mathur, P. P.; Boren, J. A.; Smyth, R. D.; Reavey-Cantwell, N. H. William H. Rorer, Inc., Research Division, Fort Washington, PA 19034 **Age differences affecting induction of hepatic drug metabolizing enzymes by methaqualone and phenobarbital in the rat.** Research Communications in Chemical Pathology and Pharmacology. 11(1):39-44, 1975.

Age differences affecting induction of hepatic drug metabolizing enzymes by methaqualone and phenobarbital were examined in the rat. Methaqualone pretreatment for 3 or 6 days caused an induction of hepatic enzymes in the young male rat as measured by a reduction in hexobarbital hypnosis. Methaqualone pretreatment had no effect on the hexobarbital hypnotic response in older male rats. Phenobarbital was a more potent enzyme inducer than methaqualone, and caused induction of liver enzymes in both age groups. 12 references. (Author abstract)

217794 Reinke, L. A.; O'Connor, M. F.; Piepho, R. W.; Stohs, S. J. Department of Medicinal Chemistry, College of Pharmacy, University of Nebraska Medical Center, Lincoln, NB 68508 **A comparison of the inductive effects of phenobarbital, methaqualone, and methyprylon on hepatic mixed function oxidase enzymes in the rat.** Research Communications in Chemical Pathology and Pharmacology. 11(1):45-53, 1975.

The effects of equal doses of three sedative hypnotics, phenobarbital, methaqualone, and methyprylon, on the hepatic mixed function oxidase enzymes of the rat were investigated and compared. After 5 days of pretreatment, phenobarbital and methyprylon significantly increased aminopyrine demethylation, aniline hydroxylation, and cytochrome P-450 content in hepatic microsomes. Methaqualone pretreatment only increased hepatic aminopyrine demethylase activity and wet liver weights. After 29 days of pretreatment, phenobarbital significantly increased aminopyrine demethylase, aniline hydroxylase activity, liver weight and cytochrome P-450 content. Methaqualone only produced a significant increase in wet liver weight. 18 references. (Author abstract)

217795 Burstein, Sumner; Varanelli, Carole; Slade, Landry T. Worcester Foundation for Experimental Biology, Shrewsbury, MA 01545 **Prostaglandins and cannabis -- III. Inhibition of biosynthesis by essential oil components of marihuana.** Biochemical Pharmacology (Oxford). 24(9):1053-1054, 1975.

The effects of cannabis on the prostaglandin synthetase activity were examined. The range of activities obtained suggested a definite structure - activity relationship for prostaglandin inhibitory activity. Results indicate that the inhibition depends on specific structural features. The role of eugenol and terpene constitutents of cannabis and myristica was also examined. 9 references.

217796 Abernathy, Charles O.; Smith, Stewart; Zimmerman, H. J. Liver Research Unit, VA Hospital, Washington, DC 20422 **The effect of chlordiazepoxide hydrochloride on the isolated perfused rat liver (38786).** Proceedings of the Society for Experimental Biology and Medicine. 129(1):271-274, 1975.

The effect of chlordiazepoxide hydrochloride (CDZ) on the isolated perfused rat liver was examined. The results demonstrated an adverse effect of CDZ on the isolated perfused rat liver. The deleterious effects of CDZ on bile flow, concentration of sulfobromopthalein (BSP) into bile and hepatic uptake of BSP were 50% greater when livers from phenobarbital (Pb) pretreated animals were used than when controls were used. However, the adverse effects of CDZ on BSP excretion were similar in both control and Pb pretreated groups. The complex interrelationship between the effects of Pb and CDZ on control livers did not permit distinction of the role of CDZ from that of a metabolite on hepatic function. 30 references.

217797 Waldeck, Bertil; Snider, Stuart R.; Brown, Roger; Carlsson, Arvid. AB Draco, Fack 5-221 01 Lund, Sweden **Studies on the synthesis and subcellular distribution of dopamine in the rad adrenal medulla.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 287(1):1-10, 1975.

The synthesis of adrenomedullary catecholamines following a pulse injection of labeled tyrosine was examined in the rat. Rats received intravenous injections of 3H-tyrosine and were killed at various time intervals thereafter. 3H-dopamine (DA) in the adrenals reached a maximum within 1.5min after the administration of 3H-tyrosine. From the fifteenth min it disappeared with an apparent half life of 90 min. 3H-adrenalin (A) and 3H-noradrenaline (NA) increased much more slowly and reached a plateau 120-240 min after the injection. In untreated animals the amount of DA and A and NA recovered from the supernatant fraction was about 10% and 8%, respectively, of the total amount recovered from the supernatant and particulate fractions. In the adrenals of animals receiving 3H-tyrosine 3.75 or 60 min beforehand these figures were significantly elevated, whereas the DA and A NA of the particulate fraction did not deviate significantly from control values. 19 references. (Author abstract modified)

217815 Grabowska, Maria; Antkiewicz, Lucyna; Michaluk, Jerzy. Institute of Pharmacology, Polish Academy of Sciences, 52 Ojcowska St., 31-344 Krakow, Poland **The influence of apomorphine and tricyclic antidepressant drugs on the level of serotonin and its metabolite in rat brain.** Biochemical Pharmacology (Oxford). 24(10):1111-1113, 1975.

The influence of tricyclic antidepressants (TAD) on the level of serotonin (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) in the brain of normal and apomorphine treated rats was examined. None of the TAD compounds, at the doses used, influenced the level of 5-HT in rat brain. The level of 5-HIAA was significantly lowered by imipramine, amitriptyline, chlorimipramine and nortriptyline. The level of 5-HIAA was not altered after administration of other doses of these compounds or after desipramine injection. The administration of apomorphine raised the level of brain 5-HT in only one experiment, but increased significantly the level of 5-HIAA in all experiments. The increase in 5-HIAA level induced by apomorphine was inhibited by all doses used of amitriptyline, chlorimipramine and imipramine, as well as by the higher of two doses of desipramine and nortriptyline. Nortriptyline depressed significantly the apomorphine induced rise in the level of 5-HT. The level of 5-HT after combined treatment with chlorimipramine and apomorphine was significantly lower than the control value. 36 references. (Author abstract modified)

217816 Morgan, William W.; Huffman, Ronald D.; McFadin, Linda S.; Yndo, Catherine A. Department of Anatomy, University of Texas Health Sciences Center, San Antonio, TX 78284 **Effect of anesthetic dosages of pentobarbital on the content and turnover of serotonin in brain areas.** Biochemical Pharmacology (Oxford). 24(10):1127-1130, 1975.

The effect of anesthetic dosages of pentobarbital on the content and turnover of serotonin in brain areas was examined in the rat. Serotonin (5-HT) content was significantly elevated in three brain areas: the medulla - pons, the midbrain, and the cerebral cortex. The rate of degradation of Serotonin (5-HT) content observed in the medulla - pons, diencephalon, midbrain and cerebral cortex after pentobarbital to 5-hydroxyindoleacetic acid 5-HIAA was significantly reduced in all six brain areas. In some brain areas, pentobarbital was observed to cause a linear exponential decrease in 5-HIAA content normally observed after monoamine oxidase inhibition. 19 references.

217817 Ben-Zvi, Zvi; Burstein, Sumner. Worcester Foundation for Experimental Biology, Shrewsbury, MA 01545 **Transformation of delta1-tetrahydrocannabinol (THC) by rabbit liver microsomes.** Biochemical Pharmacology (Oxford). 24(10):1130-1131, 1975.

The isolation and identification of two pharmacologically active metabolites of delta1-tetrahydrocannabinol (THC) by rabbit liver microsomes is reported. More than 70% of the recovered radioactivity consisted of unchanged THC. The known metabolites, 7-hydroxy-delta1-THC and 6alpha,7-hydroxy-delta1-THC, were found in thin layer chromatography zones 3 and 4 respectively; their chromatographic mobilities and gas liquid chromatography - mass spectroscopy (GLC - MS) properties were identical to those of authentic standards. Zone 2 was further separated by gas liquid chromatography into two mono-oxygenated metabolites of THC. The finding that the epoxide is not a unique metabolite of the squirrel monkey suggests that this metabolic route may also exist in man. It seems unlikely that a reactive species such as an epoxide would be a final product, raising the question of further transformation products being formed in vivo. 11 references.

217823 Ebstein, Bonnie; Roberge, Claude; Tabachnick, John; Goldstein, Menek. New York University Medical Center, Department of Psychiatry, Neurochemistry Laboratories, New York, NY 10016 **The effect of dopamine and of apomorphine on dB-cAMP-induced stimulation of synaptosomal tyrosine hydroxylase.** Journal of Pharmacy and Pharmacology (London). 26(12):975-977, 1974.

The effect of dopamine and apomorphine on dibutyryl cyclic adenosine monophosphate (dB-cAMP) induced stimulation of synaptosomal tyrosine hydroxylase was examined. The inhibitory effectiveness of dopamine was reduced from 32% to 15% by the presence of dB-cAMP in the incubation medium. Correspondingly, the percentage of stimulation of tyrosine hydroxylation elicited by dB-cAMP was increased from 54% to 94% in the presence of dopamine in the incubation medium. The inhibitory effectiveness of apomorphine was reduced from 51% to 21% in the presence of dB-cAMP in the incubation mixtures. Correspondingly, the percentage of stimulation of tyrosine hydroxylation elicited by dB-cAMP was increased from 59% to 160% in incubation mixtures with apomorphine. Haloperidol alone reduced slightly the synaptosomal tyrosine hydroxylase activity and partially reversed the inhibitory effectiveness of apomorphine. Thus, haloperidol, as well as dB-cAMP reduces the inhibitory effectiveness of apomorphine, but the effects of both compounds are not additive. The dB-cAMP elicited stimulation of synaptosomal tyrosine hydroxylase activity was not affected by haloperidol alone. However, haloperidol partially reversed the enhanced stimulation of tyrosine hydroxylase activity elicited by dB-cAMP in the presence of apomorphine. 7 references.

217824 Pernevi, Peter; Trolin, Gustaf. Department of Pharmacology, University of Goteberg, Fack, S-400 33 Goteborg 33, Sweden **Lack of effect of protriptyline on the 6-hydroxydopamine-induced noradrenaline depletion in the rat spinal cord.** Journal of Pharmacy and Pharmacology (London). 26(12):978-979, 1974.

The effect of protriptyline on the 6-hydroxydopamine (6-OH-DA) induced noradrenaline depletion in the rat spinal cord was examined. After recovery from the operation both the 6-OH-DA treated and the control animal appeared grossly normal with posture, movements and sensibility and without disturbance of urination and defecation. The noradrenaline in the spinal cord caudal to the injection site was significantly decreased in the 6-OH-DA treated groups after 30 days. There was no difference between the 6-OH-DA group pretreated with posttetanic potentiation (PTP) and that without PTP pretreatment (Table 1). The results show that 6-OH-DA injected into the tissue of the central nervous system at the concentration used here produces the same biochemical effects before and after PTP treatment. Assuming that PTP inhibits the uptake of 6-OH-DA into noradrenaline neurons, the findings indicate that the action of 6-OH-DA is not quite specific. 5-Hydroxytryptamine in the spinal cord in rats treated with 6-OH-DA in exactly the same way as in the present experiment (unpublished observations) also shows a decrease, but only down to 45% of normal values. 16 references.

217825 Hanley, M. R.; Cottrell, G. A. Department of Molecular Biology, University of California, Berkeley, CA 94720 **Acetylcholine activity in an identified 5-hydroxytryptamine containing neuron.** Journal of Pharmacy and Pharmacology (London). 26(12):980, 1974.

Acetylcholine activity in an identified 5-hydroxytryptamine containing neuron was examined. Acetylcholine activity was detected in extracts of the perikarya of the giant serotonin cell (GSC) prepared in eserinized solutions by bioassay using clam (Mya arenaria) heart strips. Extracts of filtered sea water containing one or two GSCs were forzen and thawed five or more times using liquid nitrogen to release any bound acetylcholine. The acetylcholine activity was rapidly lost in noneserinized solutions and it was destroyed in eserinized solutions by heating for 5 min at an alkaline pH. The inhibitory effect on the heart was antagonized in a quantitatively similar manner to acetylcholine by the known antagonist benzoquinonium chloride (Mytolon). 10 references.

217827 Friedman, E.; Shopsin, B.; Goldstein M.; Gershon, S. Department of Psychiatry, New York University Medical Center, 550 First Avenue, New York, NY 10016 **Interactions of imipramine and synthesis inhibitors on biogenic amines.** Journal of Pharmacy and Pharmacology (London). 26(12):995-997, 1974.

The interactions of imipramine and synthesis inhibitors on biogenic amines were examined in rats. Chronic treatment with imipramine did not alter the endogenous concentrations of brain noradrenaline, dopamine, or 5-hydroxytryptamine (5-HT). The concentrations of brain 5-hydroxyindoleacetic acid (5-HIAA), however, were significantly lowered by the treatment schedule. Alpha-methyl-para-tyrosine (MPT) treatment resulted in a significant depletion of brain noradrenaline and of dopamine, but not of 5-HT or 5-HIAA. Imipramine before and during treatment with MPT provided some protection against this depletion. However, the depletion of noradrenaline and dopamine remained statistically significant. The degree of protection was significantly less effective against dopamine depletion which was still 55% of control values. Prior and simultaneous injections of imipramine significantly, but incompletely, protected against the reduction in 5-HT and 5-HIAA concentrations. Brain concentrations of both amine and metabolite remained significantly below control values; this holds with greater significance for 5-HT. The imipramine may have exerted its protective effects on catecholamine depletion by blocking the entry of MPT into presynaptic adrenergic neurons, thus sparing the intraneuronal synthesis of catecholamine from inhibition. Alternatively, it might have retarded catecholamine metabolism. 10 references.

217837 Just, W. W.; Erdmann, G.; Thel, S.; Werner, G.; Weichmann, M. Max-Planck-Institut fur Hirnforschung, Ar-

beitsgruppe Neurochemie, D-6000 Frankfurt (Main) 71, Deutschordenstrasse 46, Germany **Metabolism and autoradiographic distribution of delta8- and delta9-tetrahydrocannabinol in some organs of the monkey Callithrix jacchus.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 287(2):219-225, 1975.

Metabolism and autoradiographic distribution of the two isomeric tetrahydrocannabinols, delta8-tetrahydrocannabinol (8-THC) and delta9-tetrahydrocannabinol (9-THC) were studied in the marmoset Callithrix jacchus. Of the two cannabinoids, 8-THC had a slower initial rate of biotransformation to the psychopharmacologically more potent 11-hydroxylated metabolite. This may explain the minor psychopharmacological activity of the 8-isomer. In glandular tissues an accumulation of unchanged 9-THC was observed. Autoradiography revealed characteristic label distributions in some organs 30 min after the administration of the drugs. This labelling pattern was found to be changed after a 6-hr incroporation period. The autoradiographic distribution of 8-THC and 9-THC appeared to be identical. 11 references. (Author abstract)

217840 Dolezalova, H.; Giacobini, E.; Giacobini, G.; Rossi, A.; Toschi, G. Laboratory of Neuropsychopharmacology, Department of Biobehavioral Sciences, University of Connecticut, Storrs, CT 06268 **Developmental variations of choline acetyl-transferase, dopamine-beta-hydroxylase and monoamineoxidase in chicken embryo and chicken sympathetic ganglia.** Brain Research (Amsterdam). 73(2):309-320, 1974.

The variations in choline acetyltransferase (ChAc) and monoamine oxidase (MAO) activity in sympathetic and spinal ganglia were studied during the postnatal development of the chicken. Dopamine-beta-hydroxylase (DBH) activity was followed throughout the prenatal and postnatal periods in sympathetic ganglia. ChAc activity in sympathetic ganglia shows a 23 fold increase between day 1 and day 7 after hatching. The activity then declines in both ganglia until day 15, and remains practically unchanged until day 30. MAO activity in sympathetic ganglia shows a significant 50% decrease on the fourth day; this activity increases to 70% of its original value by the seventh day, and remains unaltered until 30 days. No similar decrease is observed in spinal ganglia. The pattern of variation of DBH activity per protein unit in sympathetic ganglia during the prenatal period shows a peak at the eighth day of incubation. This is the period of intense proliferation of neuroblasts as well as of biochemical maturation of ganglion synapses. A subsequent increase in this activity occurs until the second day, suggesting a specific functional maturation of ganglion neurons. 30 references. (Author abstract modified)

217842 Grewaal, D. S.; Fibiger, H. C.; McGeer, E. G. Kinsmen Laboratory of Neurological Research, University of British Columbia, Vancouver, V6T 1W5, B. C., Canada **6-Hydroxydopamine and striatal acetylcholine levels.** Brain Research (Amsterdam). 73(2):372-375, 1974.

The relationship between 6-hydroxydopamine (6-OHDA) and striatal acetylcholine levels were examined in the rat. No evidence of a significant unilateral effect on striatal acetylcholine was found at various times after nigral injection of 6-OHDA or hemitransections of the brain. Results suggest that the levels on both sides might be higher and more variable than in controls. The effect seems to be transient and the lack of any unilateral effect after nigrostriatal injections of 6-OHDA suggests that the increase noted in the animals given intraventricular 6-OHDA is not a transsynaptic effect dependent upon destruction of the nigrostriatal dopaminergic tract. 7 references.

217848 Jacobowitz, David M.; Ziegler, Michael G.; Thomas, James A. Laboratory of Clinical Science, NIMH, Building 10, Room 2D-46, Bethesda, MD 20014 **In vivo uptake of antibody to dopamine-beta-hydroxylase into sympathetic elements.** Brain Research (Amsterdam). 91(1):165-170, 1975.

The capability of sympathetic elements to take up antibodies to dopamine-beta-hydroxylase (ADBH) injected into the circulation was examined in the rat. Results demonstrate that discrete structures bind with ADBH in adrenal chromaffin cells, sympathetic ganglion cell bodies and adrenergic nerve terminal fibers following i.v. administration of ADBH. The time course of this process shows that the antigen - antibody binding occurs prior to sacrifice because the presence of ADBH in sympathetic elements 10 days after injection is unlikely if a nonspecific antigen - antibody reaction was occurring during tissue sectioning. The absence of fluorescence in the superior cervical ganglia after 1 h and the minimal fluorescence observed in terminals after 15 min further argue against nonspecific antigen - antibody complex formation. It is suggested that the slow accumulation of the ADBH in all regions might be a function of the large size of the antibody molecule and its slow penetration into the synaptic cleft. Possible uptake mechanisms are discussed. 19 references.

217852 Brown, R. M.; Kehr, W.; Carlsson, A. Department of Pharmacology, University of Goteborg, Goteborg, Sweden **Functional and biochemical aspects of catecholamine metabolism in brain under hypoxia.** Brain Research (Amsterdam). 85(3):491-509, 1975.

The functional and biochemical aspects of catecholamine metabolism were examined in the rat brain. Animals exposed to 6% oxygen showed a partial inhibition of the rate of tyrosine hydroxylation and a blockade of the conditioned avoidance response. The behavioral disruption was suggested to result, at least in part, from a dopaminergic disturbance, since the behavior was restored by the administration of DOPA or apomorphine but not by 5-hydroxytryptophan. Biochemical data showed a selective retardation in brain dopamine (DA) disappearance after synthesis inhibition. Methoxytyramine formation was markedly retarded. Analysis of this effect indicate that the decreased DA turnover was related to the release of transmitter rather than to an effect on catechol-O-methyltransferase (COMT) or monoamine oxidase (MAO). In addition, there was evidence for a partial inhibition of MAO activity by hypoxia as well as a decreased activity of dopamine-beta-hydroxylase. It is concluded that the disruption of behavior was related to decreased dopaminergic receptor activation and that decreased synthesis played at most a contributory role. 44 references. (Author abstract)

217853 Hanbauer, I.; Guidotti, A.; Costa, E. Section on Biochemical Pharmacology, Hypertension Endocrine Branch, National Heart and Lung Insitute, N. I. H., Bethesda, MD 20014 **Dexamethasone induces tyrosine hydroxylase in sympathetic ganglia but not in adrenal medulla.** Brain Research (Amsterdam). 85(3):527-531, 1975.

Dexamethasone induced tyrosine hydroxylase (TH) was examined in the sympathetic ganglia and the adrenal medulla of the rat. The TH activity in superior cervical ganglia of rats injected with dexamethasone increased after a time latency longer than 24 hr, and the increase was dose dependent. In contrast, the TH activity in the adrenal medulla was not affected. When dexamethasone was injected into rats which had been unilaterally decentralized, the drug failed to increase the TH activity in the ganglion. The results indicate that the drug requires an intact innervation. In addition, cortexolone failed

to inhibit the TH induction elicited by l-epinephrine. The results also indicate that the inhibition of TH induction by cortexolone is specific for the induction elicited by dexamethasone. 18 references.

217854 Brooke, Sheila M.; Fibiger, Hans C. Division of Neurological Sciences, Department of Psychiatry, University of British Columbia, Vancouver, B. C., Canada **Differential rates of increase in pontine tyrosine hydroxylase and dopamine-beta-hydroxylase activities after reserpine.** Brain Research (Amsterdam). 85(3):532-534, 1975.

Differential rates of increase in pontine hydroxylase and dopamine-beta-hydroxylase (DBH) activities after reserpine were examined in rats. Reserpine significantly increased tyrosine hydroxylase (TH) activity in the brainstem. The pontine tyrosine hydroxylase activity was still significantly elevated 12 days after the injection. Dopamine-beta-hydroxylase activity was not significantly different from that of controls. The results indicate that DBH activity in the brain can like tyrosine hydroxylase be increased by reserpine. The latency of the reserpine induced increase in DBH was greater than that required to increase TH. It is suggested that different factors determine the rate of synthesis or turnover of tyrosine hydroxylase and TH and DBH in central noradrenergic neurons. 12 references.

217858 Battistin, Leontino; Varotto, Mary; De Lorenzi, Aldo. Clinica delle Malattie Nervose e Mentali, Universita di Padova, Padua 35100, Italy **Amino acid uptake in vivo by the mouse brain and by various regions of the rabbit brain after drug-induced convulsions.** Brain Research (Amsterdam). 89(2):215-224, 1975.

The levels of the free amino acids of the mouse brain were studied after convulsions induced by Metrazol. A decrease of level of taurine and a significant increase of level of alanine, phenylalanine and isoleucine were found. The net uptake of L-histidine by the mouse brain in vivo was similar under normal conditions and after Metrazol induced generalized convulsions; that of L-methionine was much higher after convulsions and there was no uptake of L-aspartic acid, either under physiological conditions or after convulsions. The net uptake of L-histidine by various regions of the rabbit brain in vivo after convulsions was significantly higher than control values in the cortical areas, while that of L-methionine was significantly higher in the subcortical ones; there was no uptake of L-aspartic acid by the rabbit brain in normal condition, whereas after convulsions a small entry seemed to occur in the subcortical areas. These results indicate that cerebral permeability processes of amino acids are somewhat altered during convulsive phenomena, as already described elsewhere for ions and proteins. 28 references. (Author abstract)

217863 Mosko, Sarah S.; Jacobs, Barry L. Department of Psychology, Princeton University, Princeton, NJ 08540 **Midbrain raphe neurons: sensitivity to glucocorticoids and ACTH in the rat.** Brain Research (Amsterdam). 89(2):368-375, 1975.

The effect of corticosteroids on raphe unit activity was studied in intact and adrenalectomized (ADX) male Sprague-Dawley rats. The data indicate that the mechanism by which brain serotonin is regulated, on a short-term basis, by or glucocorticoids does not involve modulation of the adrenocorticotropic hormone (ACTH) neuronal activity of serotonin containing cells. Midbrain raphe units in intact and ADX animals were typically unresponsive to elevations in plasma corticosterone. The fact that no cells responded to the lowest dose is particularly relevant since this dose produced an elevation in plasma corticosterone levels within the physiological range of the animal. Therefore, raphe cells generally appear insensitive to a physiological increase in circulating corticosterone, as well as to the administration of high doses which probably elevate plasma corticosterone beyond physiological limits. The failure of raphe neurons to respond to ACTH or glucocorticoids also suggests that the reported activation of 5-hydroxytryptamine (5-HT) metabolism following stressors does not reflect increased neuronal activity in 5-HT containing neurons in response to the hypersecretion of pituitary and adrenal hormones. 37 references.

217865 Foote, Stephen L.; Freedman, Robert; Olivier, A. Paul. Laboratory of Neuropharmacology, Div. of Special Mental Health Research, NIMH, St. Elizabeth's Hospital, Washington, DC 20032 **Effects of putative neurotransmitters on neuronal activity in monkey auditory cortex.** Brain Research (Amsterdam). 86(2):229-242, 1975.

The effects of the putative neurotransmitters norepinephrine (NE), gamma-aminobutyric acid (GABA), and acetylcholine (ACh) were tested on auditory cortex neurons which were activated acoustically by species specific vocalizations in awake squirrel monkeys. Dose dependent inhibition of spontaneous and vocalization evoked discharge rates was seen with NE and GABA. Generally, excitation was observed with ACh. A given dose of NE or GABA reduced spontaneous activity by a greater proportion than it reduced activity evoked by vocalizations. During excitatory responses, segments with lower discharge rates were reduced proportionately more than segments with higher discharge rates. The demonstration that small amounts of locally applied NE and GABA substantially alter the specific neuronal activation produced by vocalizations provides additional evidence that these agents may function as neurotransmitters in this neocortical area and offers clues about their functional significance. 45 references. (Author abstract modified)

217867 Zieher, Luis M.; Jaim-Etcheverry, Guillermo. Instituto de Biologia Celular, Facultad de Medicina, Buenos Aires, Argentina **6-Hydroxydopa during development of central adrenergic neurons produces different long-term changes in rat brain noradrenaline.** Brain Research (Amsterdam). 86(2):271-281, 1975.

The effect of 6-hydroxydopa (6-OH-DOPA) administered to rats during their early development on the content of brain noradrenaline (NA) was examined. An increase in brain stem NA is observed when the rats are exposed to the drug between the day 14 of gestation and 9th postnatal day. When 6-OH-DOPA is injected subcutaneously on the 13th postnatal day or later, there is a decrease in brainstem NA. The content of NA in the telediencephalon is depleted for the first time in rats exposed to the drug during the day 16 of gestation, the decrease is more evident when the injection is done on days 17 or 18 and the effect is also marked when the drug is administered in the period between the day of birth and the 20th day of age. These results indicate that 6-OH-DOPA exerts different effects during the process of development and that the increase in brainstem NA is not solely dependent on the depletion produced in the forebrain because both phenomena are temporarily dissociated. 36 references. (Author abstract modified)

217869 Barker, L. A.; Dowdall, M. J.; Mittag, T. W. Department of Pharmacology, Mount Sinai School of Medicine, CUNY, New York, NY 10029 **Comparative studies on synaptosomes: high-affinity uptake and acetylation of N-(Me-**

3H)choline and N-(Me-3H)N-hydroxyethylpyrrolidinium. Brain Research (Amsterdam). 86(2):343-348, 1975.

The relationship between the high affinity uptake and acetylation of choline and analogs was examined in the squid (Loligo pealii) and the rat. The high affinity choline transport system present in synaptosomes isolated from squid optic lobes was similar in many ways to its counterpart in synaptosomes prepared from rat forebrain. The affinities of two substrates, choline and pyrrolcholine, for the carrier are essentially the same in both synaptosomal preparations. The major difference between the two species with respect to choline metabolism by synaptosomes is in the relationship between the high affinity transport and subsequent acetylation of choline and pyrrocholine. Alternatively, if a coupling mechanism is operative in squid synaptosomes, the extent of coupling is not as great as is seen with the synaptosomes isolated from rat brain. The comparative studies on choline transport in squid and rat synaptosomes suggest that the relationship between high affinity transport and acetylation may not be the same for all cholinergic terminals. 14 references.

217872 Ben-Ari, Yehezkel; Zigmond, Richard E.; Moore, Kenneth E. Neurochemical Pharmacology Unit, Department of Pharmacology, Hills Road, Cambridge CB2 2QD, England **Regional distribution of tyrosine hydroxylase, norepinephrine and dopamine within the amygdaloid complex of the rat.** Brain Research (Amsterdam). 87(1):96-101, 1975.

The regional distribution of tyrosine hydroxylase, norepinephrine, and dopamine within the amygdaloid complex was examined in the rat. The enzyme activity was 4-5 times higher in the basolateral amygdala (B) than in the anteromedial amygdala (AM), independent of the level of the section. This observation was confirmed in 18 out of 19 BL and AM samples from seven rats. Within the amygdaloid complex the central nucleus had the highest tyrosine hydroxykese activity. Enqyme activity in the pyriform cortex was slightly higher in the AM while tyrosine hydroxylase activity was very high in the area of the caudate putamen adjoining the amygdala. The same regions, plus the anterior anygdala, were analyzed for norepinephrine and dopamine. All regions examined except the caudate putamen contained norepinephrine. The concentrations of this amine in the basolateral and central nuclei were approximately twice the amount in the corticomedial and anterior amygdala and in the pyriform cortex. The distribution of dopamine was rather different from that of norepinephrine. 14 references.

217873 Suria, Amin; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital Washington, DC 20032 **Action of diazepam, dibutyryl cGMP, and GABA on presynaptic nerve terminals in bullfrog sympathetic ganglia.** Brain Research (Amsterdam). 87(1):102-106, 1975.

The action of diazepam, dibutyryl cyclic guanosine monophosphate (diB-cGMP) and gamma-aminobutyric acid (GABA) on presynaptic nerve terminals were examined in bullfrog sympathetic ganglia. Neither cyclic adenosine monophosphate (cAMP) hor cGMP changed the membrane potential recorded from the preganglionic nerve endings, or from the interganglionic nerve trunk. The dibutyryl derivative of cAMP was also ineffective on both responses; however, diB-cGMP depolarized the preganglionic nerve terminals. Picrotoxin failed to change the polarization of presynaptic terminal membranes and antagonized the depolarization elicited by equimolar concentrations of diazepam. Glycine or glutamic acid neither depolarized the presynaptic nerve terminals nor changed the amplitude of the antidromic action potential. Results show that diazepam and diB-cGMP depolarize the preganglionic nerves located within the ganglion. It is suggested that diazepam and diB-cGMP inhibit the posttetanic potentiation by depolarizing the presynaptic nerve terminals. 15 references.

217874 Banna, N. R.; Kurkjian, R. School of Pharmacy, American University of Beirut, Beirut, Lebanon **A novel tremorigen antagonized by D-amphetamine.** Brain Research (Amsterdam). 87(1):114-117, 1975.

A new type of chemical structure possessing centrally induced tremorigen activity, and showing a different spectrum of pharmacological activity, and called 2-thiophenecarboxaldehydeoxime (THAO) was examined. In order to determine the role of various levels of the neuraxis in mediating THAO induced tremor, cats were hemidecorticated, the other hemisphere being exposed without decortication and serving as a control. In these rats, THAO induced tremors in all four limbs, which excluded a cortical site of action. Complete decortication also failed to block the tremorigenic action in cats, although tremor became coarser. Midcollicular decrebration, however, performed on four cats under ether anesthesia, blocked the tremorigenic action when THAO was administered 2 h after cessation of anesthesia. The tremorigenic and depressant effects of THAO were effectively reduced by pretreatment of the mice, 30-60 min prior to its administration, with D-amphetamine sulfate (10mg/kg). In the presence of amphetamine, larger doses of THAO were required for the production of well defined tremors. Furthermore, the duration of tremor in amphetamine pretreated mice evoked by the higher doses of THAO was considerably reduced. 6 references.

217879 Fuller, Ray W.; Baker, John C. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN **Long-lasting reduction of brain 5-hydroxytryptamine concentration by 3-chloroamphetamine and 4-chloroamphetamine in iprindole-treated rats.** Journal of Pharmacy and Pharmacology (London). 26(11):912-914, 1974.

A long-lasting reduction of brain 5-hydroxytryptamine concentration by 3-chloroamphetamine and 4-chloroamphetamine in iprinole treated rats is reported. The results indicate that 3-chloroamphetamine is like 4-chloroamphetamine not only in having the ability to lower 5-hydroxyindole concentrations at short times, but also at a long time (1 week) after drug treatment, when differences in metabolism between the two drugs are eliminated by treatment with iprindole to block ring hydroxylation. If some active metabolite is required for the long-term effect, the metabolite can apparently be formed from both drugs after iprindole treatment. It is hypothesized that the postulated neurotoxic metabolite may be produced in the 5-hydroxytryptamine neuron. Whereas iprindole can inhibit the ring hydroxylation of amphetamines by rat liver, there is no reason to believe that iprindole would alter any metabolic transformation of the chloroamphetamines in brain neurons. 8 references.

217881 Jonsson, John; Lewander, Tommy. Psychiatric Research Center, University of Uppsala, Ullerakers Hospital, S-750 17 Uppsala, Sweden **Effects of the dopamine-beta-hydroxylase inhibitor FLA 63 on the kinetics of elimination of amphetamine in the rat.** Journal of Pharmacy and Pharmacology (London). 26(11):907-909, 1974.

An interaction between FLA 63 (bis-1-methyl-4-homopiperazinylthiocarbonyl) disulphide and amphetamine in rats is reported. FLA 63 administered 1 h before amphetamine

significantly prolonged the amphetamine induced increase in motor activity by approximately 2.5h. Pretreatment with FLA 63 significantly increased the concentration of brain amphetamine at 2 and 4 h after amphetamine when the rats were pretreated with FLA 63. The effect of FLA 63 seemed to be dose dependent at this time interval after the injection of amphetamine. Of all the tissues, the increase in the amphetamine concentration after pretreatment with FLA 63 was most pronounced in plasma. The duration of the amphetamine induced increase in motor activity followed roughly the concentration of amphetamine in brain and plasma. The results demonstrate that FLA 63 pretreatment interferes with the kinetics of elimination of amphetaminc, which is associated with a prolongation of one of its pharmacological effects. 9 references.

217882 Hughes, I. E.; Kneen, Barbara; Main, Vivian A. Department of Pharmacology, Medical School, Thoresby Place, Leeds LS2 9NL, Yorkshire, England **The use of desipramine in studies of noradrenergic nerve function.** Journal of Pharmacy and Pharmacology (London). 26(11):903-904, 1974.

The use of desipramine in studies of noradrenergic nerve function was evaluated. The net effect of desipramine on the response to noradrenaline in guinea-pig and mouse vasa deferentia proved to be a balance between potentiation due to uptake blockade and antagonism due to alpha-adrenoceptor blockade. Desipramine was highly effective as an alpha-adrenoceptor blocking agent in mouse vas deferens and this action overrode the potentiation due to uptake blockade; thus a net reduction in the response was seen. In guinea-pig vas deferens, however, the lower alpha-adrenoceptor blocking activity of desipramine enabled a net potentiation to be produced. The results have implications for the use of desipramine as a tool to block noradrenaline uptake in investigations of the nature of the control over the release of noradrenaline. 7 references.

217885 Schain, Richard J.; Watanabe, Kathy. Department of Pediatrics, University of California, Center for the Health Sciences, Los Angeles, CA 90024 **Effect of chronic phenobarbital administration upon brain growth of the infant rat.** Experimental Neurology. 47(3):509-515, 1975.

The effect of chronic phenobarbital administration upon brain growth of the infant rat was examined. Administration of 0.06mg/g of phenobarbital daily to infant rats during the first 3 weeks of life retarded body and brain growth during this period. Analysis of data suggests that these effects are not solely due to impaired nutrition. Accumulation of cholesterol in the cerebellum was slowed to a greater extent than was accumulation of other brain constituents measured (deoxyribonueleic acid, ribonucleic acid, and protein). These findings raise the possibility that chronic administration of pheonbarbital delays brain development of infant rats. 13 references. (Author abstract)

217888 Zivkovic, B.; Guidotti, A.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeth's Hospital, Washington, DC 20032 **Stereospecificity of dopamine receptors involved in the regulation of the kinetic state of tyrosine hydroxylase in striatum and nucleus accumbens.** Journal of Pharmacy and Pharmacology (London). 27(5):359-360, 1975.

Stereospecificity of dopamine receptors in the regulation of the kinetic state of tyrosine hydroxylase (TH) in striatum and nucleus accumbens was examined in the rat. Butaclamol, injected into rats 30 min before decapitation, decreased the apparent Km of striatal TH for 2-amino-4-hydroxy-6,7-dimethyltetrahydropterine (DMPH) by about 4.5times. The Km of the enzyme for tyrosine was not affected. Butaclamol was almost equipotent in increasing TH activity in striatum and nucleus accumbens. In contrast, 400 times higher dose of (-)-butaclamol failed to produce significant change in TH activity in both regions investigated. Thus, the dopamine receptor that is involved in the regulation of the kinetic state of TH appears to be highly stereospecific. Results suggest that the receptor which mediates the regulation of the kinetic state of TH present in dopaminergic neurons and the receptor which is involved in the regulation of some behavioral patterns have similar, if not identical, steric configuration. It appears that the receptors in striatum and in nucleus accumbens have similar affinity for the enantiomers of butaclamol. 11 references.

217889 Paton, D. M. Department of Pharmacology, University of Alberta, Edmonton, Alberta, Canada T6G 2E1 **Effect of amphetamine, 3,4-methylenedioxyamphetamine, p-methoxyamphetamine and related amphetamines on uptake of metaraminol and efflux of noradrenaline in adrenergic nerves of rabbit atria.** Journal of Pharmacy and Pharmacology (London). 27(5):361-362, 1975.

The effects of 3,4-methylenedioxyamphetamine (MDA) and p-methoxyamphetamine (PMA) on the uptake and efflux of catecholamines in peripheral adrenergic nerves were examined in the rabbit. Both (+)-amphetamine and (-)-amphetamine were potent inhibitors of the uptake of (3H)(0)-metaraminol. MDA and PMA also produced very significant inhibition of uptake, MDA being slightly more potent. By contrast, the dimethoxyamphetamine derivatives studied were much weaker inhibitors of uptake only the 2,3, 2,4 and 3,5 derivatives produced significant inhibition of uptake but all were less potent than amphetamine, MDA and PMA. Amphetamine and MDA both caused considerable acceleration of the efflux of (3H)noradrenaline from rabbit atria and were approximately equipotent. PMA proved to be less potent. The dimethoxyamphetamine derivatives did not alter the efflux of (3H)(-)-noradrenaline significantly. 9 references.

217890 Buczko, W.; deGaetano, G.; Garattini, S. Department of Pharmacology, Medical School, Bialystok, Poland **Effect of some anorectic agents on the uptake and release of 5-hydroxytryptamine by blood platelets of rats.** Journal of Pharmacy and Pharmacology (London). 27(5):366-368, 1975.

The effect of some anorectic agents on the uptake of and release of 5-hydroxytryptamine (5-HT) by blood platelets of rats was examined in the rat. Phentermine, diethylpropion, SKF 39728-A and (+)-amphetamine were not capable of inhibiting 5-HT uptake and neither were they able to release 5-HT from rat platelets in vitro, as does fenfluramine. S 992, a congener of fenfluramine, was inactive as an inhibitor of 5-HT uptake, while it was a weak releaser of 5-HT from platelets. Mazindol was comparable to fenfluramine in its capacity to inhibit 5-HT uptake but it too was a weak releaser of 5-HT. 4-Chloroamphetamine was more effective than fenfluramine on both parameters. The results indicate that the in vivo effects of anorectic drugs on brain 5-HT concentrations are better correlated with the capacity of these drugs to release 5-HT from platelets in vitro that with their inhibitory activity on platelet 5-HT uptake. 12 references.

217891 Sharples, D. Department of Pharmacy, The University, Manchester, M13 9PL, England **Competition for plasma protein binding sites between phenothiazine tranquilizers and iminodibenzyl antidepressants.** Journal of Pharmacy and Pharmacology (London). 27(5):379-381, 1975.

Competition for plasma protein binding sites between phenothiazine tranquilizers and iminodibenzyl antidepressants was examined. The results indicate that the number of binding sites for iminodibenzyl antidepressants is not significantly altered by the presence of phenothiazine tranquilizers. The affinity of binding however is greatly reduced by the presence of phenothiazine tranquilizers. Phenothiazines do therefore displace iminodibenzyl antidepressants from protein binding sites in vitro and the competition is reversible. Phenothiazines displace iminodibenzyl compounds and not vice versa since the affinities of the phenothiazines are always greater. The extent to which displacement occurs seems therefore to be related to the relative affinities of the two compounds concerned. The greater the difference between the two affinities, the greater will be the amount of displacement. 10 references.

217897 Meisch, Jean-Jacques; Waldeck, Bertil. Netherlands Central Institute for Brain Research, Amsterdam **Uptake and disappearance of 4-mthyl-alpha-ethylmetatyramine in relation to its releasing action on 5-hydroxytryptamine in the brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 287(3):233-242, 1975.

The metabolism of 4-methyl-alpha-ethylmetatyramine (H75/12X) was examined in ralation to its releasing action of 5-hydroxytryptamine in the rat brain. H75/12 was rapidly taken up by the heart and then disappeared biphasically or multiphasically. A maximum concentration was obtained in the brain 30-60 min after the administration of 25mg/kg. H75/12 disappeared from the brain with a halflife of 1.0and 1.5hrs in the mouse and rat, respectively. In the mouse the relative uptake of H75/12 increased with the dose given, i.e. the dose uptake curve had an upward bending. Significant relase of serotonin (5-HT) in the brain was obtained after a single injection of 25 and 100mg/kg in the rat and mouse, respectively. The 5-HT release was prevented by tricylcic, antidepressive agents, particularly by chlorimipramine. It is concluded that only a minor part of the H75/12 measured is located in monoaminergic neurons. The uptake of H75/12 in the rat brain appeared to be increased in starving animals, possibility decreased metabolism of the drug. (Author abstract modified)

217961 Brown, F.; Redfern, P. H. School of Pharmacy and Pharmacology, University of Bath, Bath, England **The effect of amantadine on the turnover of catecholamines in the rat brain.** Journal of Pharmacy and Pharmacology (London). 26(Suppl.):81P-82P, 1974.

The effect of amantadine on the turnover of catecholamines in the brain following alpha-methyl-p-tyrosine administration was examined in the rat. Amantadine did not significantly affect dopamine (DA) turnover, but produced a slight but significant increase in the rate of decline of noradrenalin (NA) concentrations. Rates of decline of both NA and DA concentrations in the brains of rats treated for 9 days with amantadine in the drinking water were not significantly different from those in the brains of control animals. The lack of effect of amantadine in this experimental situation, when compared to the effectiveness of other drugs, all of which are believed to stimulate or block dopamine receptors, suggests that amantadine does not owe its antiparkinson properties to a postsynaptic action at dopaminergic synapses in the central nervous system. 10 references.

217962 Joseph, Christopher; Tonge, Sally R. School of Pharmacy, Liverpool Polytechnic, Byrom Street, Liverpool L3 3AF, England **Some interactions between fenfluramine and antidepressant drugs: effects on 5-hydroxyindole concentrations in rat brain.** Journal of Pharmacy and Pharmacology (London). 26(Suppl.):91P, 1974.

Interactions between fenfluramine and antidepressants were examined with respect to effects on 5-hydroxytryptamine metabolism. Fenfluramine alone was found to reduce 5-hydroxytryptamine levels in whole rat brain and also caused a slight reduction of 5-hydroxyindoleacetic acid concentrations. The same dose of fenfluramine antagonized the effects of imipramine, iproniazid and amphetamine on both 5-hydroxytryptamine elevating effect of a combination of reserpine and the 5-hydroxytryptamine elevating effect of a combination of reserpine and iproniazid. These results indicate that, far from having a reserpine like effect on 5-hydroxytryptamine metabolism, fenfluramine may stabilize the intraneuronal storage granules (the stable pool). A stabilization of the storage granules might prevent the incorporation of newly synthesized 5-hydroxytryptamine and also the reuptake mechanism; such an effect could explain both the depletion of 5-hydroxytryptamine and the increase in its turnover rate described by other authors. 4 references.

217963 Tonge, Sally R. School of Pharmacy, Liverpool Polytechnic, Byrom Street, Liverpool L3 3 AF, England **Changes in the concentrations of 5-hydroxytryptamine and noradrenaline in six areas of rat brain during recovery from chronic methylamphetamine administration.** Journal of Pharmacy and Pharmacology (London). 26(Suppl.):91P-92P, 1974.

Changes in the concentrations of 5-hydroxytryptamine and noradrenaline were examined in six areas of rat brain during recovery from chronic methylamphetamine administration. When compared with littermate untreated rats, noradrenaline concentrations were found to have been reduced in all areas of the brain by chronic methylamphetamine administration; 5-hydroxytryptamine concentrations were also reduced in the striatum and midbrain, but were unaltered in the thalamus/hypothalamus, the hippocampus and the pons/medulla, and were increased in the cortex. In all areas except the striatum, 5-hydroxytryptamine concentrations were lower 24 hours than 0 hours after withdrawal. These results suggest that chronic methylamphetamine ingestion may affect not only the release of monoamines, but also their synthesis and transport along neuronal axons. They also suggest a biochemical basis for the marked postamphetamine depression frequently reported in man. 3 references.

217964 Ahtee, Liisa. Department of Pharmacology, University of Helsinki, Siltavuorenpenger 10, SF-00170, Helsinki 17, Finland **Dextromethorphan inhibits 5-hydroxytryptamine uptake by human blood platelets and decreases 5-hydroxyindoleacetic acid content in rat brain.** Journal of Pharmacy and Pharmacology (London). 27(3):177-180, 1975.

The effect of dextromethorphan on the uptake and metabolism of 5-hydroxytryptamine (5-HT) was studied in human blood platelets and in rat brain. In the concentration of 120nM dextromethorphan inhibited the uptake of 5-HT into platelets by 50%. The corresponding concentrations of imipramine and methadone under similar conditions were 22 and 590nM, respectively. Dextromethorphan decreased the concentration of brain accumulation of 5-hydroxyindoleacetic acid (5-HIAA) time and dose dependently. However, dextromethorphan did not alter the pargyline induced changes in brain 5-HT metabolism. Dextromethorphan induced changes in brain 5-HT metabolism could arise from the inhibition of the reuptake of 5-HT into neurons. 20 references. (Author abstract)

217965 Ulus, I. H.; Kiran, B. K. Department of Pharmacy and Clinical Pharmacology, Bursa Medical School, Bursa, Turkey **The effect of 6-hydroxydopamine on the tolerance development to the hyperthermic effect of (+)-amphetamine in the rat.** Journal of Pharmacy and Pharmacology (London). 27(3):205-206, 1975.

The effect of 6-hydroxydopamine (6-OH-DA) on the tolerance development to the hyperthermic effect of (+)-amphetamine in the rat was examined. The increase in body temperature of 6-OH-DA pretreated rats was significantly lower than the increase in temperature of control rats on the first day of (+)-amphetamine administration. With time, the increase in body temperature gradually decreased in the 6-OH-DA pretreated animals until there was no difference between the rectal temperature of saline controls and of (+)-amphetamine treated rats on the 20th day. In the vehicle injected rats no difference was observed in the temperature responses to (+)-amphetamine injection on the 1st, 12th and 20th days. According to these results it would appear that (+)-amphetamine induced hyperthermia may be due to some central catecholaminergic mechanisms rather than peripheral mechanisms, because the selective elimination of central catecholamines by intraventricular 6-OH-DA facilitated the tolerance development to the hyperthermic effect of (+)-amphetamine. 10 references.

217966 Nielsen, M. Sct. Hans Hospital, Central Laboratory, Dept. E., DK-4000 Roskilde, Denmark **The influence of desipramine and amitriptyline on the accumulation of (3H)noradrenaline and its two major metabolites formed from (3H)tyrosine in the rat brain.** Journal of Pharmacy and Pharmacology (London). 27(3):206-209, 1975.

The influence of desipramine and amitriptyline on the accumulation of (3H)-noradrenaline (3H-NA) and its two major metabolites formed from (3H)tyrosine in the rat brain was examined. Pretreatment with desipramine led to a decreased formation of 3H-NA and its two labelled metabolites after the intravenous injection of (3H)tyrosine. This strong indication of inhibition of total brain noradrenaline synthesis was not found after a high dose of amitriptyline. A similar conclusion was obtained after the intraventricular injection of (3H)-tyrosine. However, the brain concentrations of 3H-NA showed less pronounced decreases after the intraventricular injections compared with the intravenous administration. Desipramine induced no significant decrease in 3H-NA at low doses whereas at 20mg/kg it produced a significant decrease. The present results provide strong direct evidence that the secondary amine desipramine but not the tertiary amine amitriptyline decreases total brain synthesis of noradrenaline, since both 3H-NA and its major metabolites were decreased after desipramine. 12 references.

218047 Hofer, Myron A.; Weiner, Herbert. Department of Psychiatry, Albert Einstein College of Medicine at Montfiore Hospital, 111 E. 210th St., Bronx, NY 10467 **Physiological mechanisms for cardiac control by nutritional intake after early maternal separation in the young rat.** Psychosomatic Medicine. 37(1):8-24, 1975.

Series of analytic experiments are presented that explore possible physiological mechanisms for the control of cardiac rate by nutritional intake in the preweanling rat. The essential properties for the nutrient and the first site of action were studied by using fluids of different pH, osmolality and chemical composition. Several probable effector pathways were explored: neuroendocrine, cholinergic, and adrenergic. Pharmacological blocking agents, surgical removal of glands, replacement hormones and spinal cord transection were utilized. Afferent pathways such as vagus and splanchnic systems were approached surgically and the gastrointestinal hormones, histamine, insulin and glucagon were studied by administration and pharmacologic blockade. The evidence tended to rule out a number of possible mechanisms and pathways and to make it appear likely that nutrient acts initially at the gut wall, that the central nervous system then responds by increasing tone in the classical spinal cardioacceleratory pathways to the beta-adrenergic synapses of myocardium. 20 references. (Author abstract modified)

218147 Ziegler, Michael G.; Thomas, James A.; Jacobowitz, David M. Laboratory of Clinical Science, Bldg. 10 Room 2D-46, NIMH, Bethesda, MD 20014 **In vivo binding of antibody to dopamine-beta-hydroxylase in adrenergic nerves and subsequent antidromic transport (Unpublished paper).** Bethesda, MD, NIMH, 1975, 1 p.

The in vivo binding of antibody to dopamine-beta-hydroxylase (DBH) in adrenergic nerves and subsequent antidromic transport is investigated. A specific antibody to DBH was injected into rats and the binding of anti-DBH (ADBH) to sympathetic cells was studied. Results show that ADBH can bind to intracellular structures in living animals and that after it is taken up at nerve terminals, it can be transported by an antidromic flow to the nerve cell body. (Author abstract modified)

218148 Padjen, Ante; Bloom, Floyd. Laboratory of Neuropharmacology, Div. of Special Mental Health Research, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Problems in the electrophysiological analysis of the site of action of benzodiazepines. (Unpublished paper).** Washington, DC, NIMH, 1975, 17 p.

A literature study of the electrophysiological data on the analysis of the actions of benzodiazepines with microelectrodes and macroelectrodes is reported, and an attempt to integrate these data from various brain regions into possibly testable hypotheses of electrophysiological effects is made. The action of the drug on animals and humans is compared. It is suggested that benzodiazepines can affect several neurotransmitter neuronal systems and that they may be able to supress the corollary extension of sensory information from the primary sensory systems into more associative sensory systems. It is also suggested that gamma-aminobutyric acid mediated actions may play an essential role in the spinal effects of benzodiazepines especially through the facilitation of presynaptic inhibition. The GABA hypothesis for benzodiazepines is discussed. Suggestions for future research are included. 49 references.

218149 Costa, E.; Guidotti, A.; Mao, C. C. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **A "GABA hypothesis" for the action of benzodiazepines. (Unpublished paper).** Washington, DC, NIMH, 1975, 31 p.

The participation of gamma-aminobutyric acid (GABA)-ergic neurons in the mediation of the action of diazepam and other benzodiazepines in the cerebellum was studied. The measurement of changes in cerebellar concentrations of 3',5'-cyclic guanosine monophosphate (cGMP) associated with pharmacologically induced modifications of GABA-ergic transmission is taken as an index of such a participation. Studies suggest the following: that diazepam appears to act like GABA because it counteracts the consequences of a GABA deficit; there is no direct action of GABA on guanylcyclase but a

change in cGMP effects associated with changes in GABA-ergic function is a reflection of the indirect action of GABA on the release of other transmitters; diazepam, by acting on the Purkinje cells counteracts the actions of the excitatory transmitter which is released by the climbing fibers or by other fibers and controls the cGMP content of Purkinje cells; and either the cerebellar guanylcyclase of Purkinje cells or the cyclic nucleotide phosphodiesterase of these cells may be regulated by the excitatory transmitter released from the climbing fibers. 33 references.

218164 Cahn, J.; Herold, M.; Borzeix, M. G. Institut de Therapeutique Experimentale et de Recherches Cliniques, 6, rue Blanche, 92120 Montrouge, France /**Pharmacology of cerebral circulation and clinical applications. Experimental study of the circulatory and metabolic effects of Hydrosarpan 711.**/ Pharmacologie de la circulation cerebrale et extrapolations cliniques. Etude experimentale des effets circulatoires et metaboliques d'Hydrosarpan 711. Semaine des Hopitaux Therapeutique (Paris). 50(10):671-682, 1974.

The activity of Hydrosarpan 711 was investigated with several experimental models of cerebral vascular - metabolic pathology. On the hemodynamic level, Hydrosarpan maintains autoregulation of the cerebral output in the hypertensive dog whatever the variations in tension. Its effect is not vasodilatatory since it suppresses vasoparalytic dilation anoxia and tissue acidosis. On the cerebral metabolic level, it increases the cerebral contribution of oxygen and the brain's consumption of oxygen; it reduces lactic acidosis and pCO2 variations which accompany it. It possesses a clear cerebral antiedema effect. Hydrosarpan 711 seems particularly suitable for treating the cerebral - sensory disturbances of arterial hypertension and cerebral atherosclerotic circulatory insufficiency. 10 references. (Journal abstract modified)

218190 Fairchild, M. D.; Jenden, D. J.; Mickey, M. R. Department of Pharmacology, U.C.L.A. School of Medicine, Los Angeles, CA 90024 **An application of long-term frequency analysis in measuring drug-specific alterations in the EEG of the cat.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 38(4):337-348, 1975

A method for the quantitative measurement of drug specific effects on the electroencephalogram (EEG) of the cat is described. These effects are dose related and are independent of the normal sources of EEG variation associated with the sleep - waking cycle. Drug induced changes are expressed as characteristic alterations in frequency spectra and the time courses of these effects are followed for 5 h following administration of the test compounds. Broad band frequency analysis of spontaneous brain activity of cats under atropine sulfate and physostigmine salicylate was subjected to discriminant and canonical statistical analysis programs and it was determined that both atropine and physostigmine produce alterations in EEG frequency spectra which are clearly distinct from those patterns associated with the sleep - waking cycle. 34 references. (Author abstract modified)

218191 Racine, Ronald; Livingston, Kenneth; Joaquin, Andrew. Department of Psychology, McMaster University, Hamilton, Ontario **Effects of procaine hydrochloride, diazepam, and diphenylhydantoin on seizure development in cortical and subcortical structures in rats.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 38(4):355-365, 1975.

The effects of procaine HCl, diazepam, and diphenylhydantoin (DPH) on kindled seizures in hooded rats were investigated. Procaine HCl and DPH increased the duration and propagation of epileptiform discharges (ADs) produced by electrical stimulation of the amygdala in rats. Procaine and DPH also increased the rate of seizure development (kindling) produced by repeated stimulation of the amygdala. Procaine acted as a convulsant in well kindled Ss. Diazepam retarded or blocked amygdaloid kindling, and triggered a high frequency rhythm in the amygdala, hippocampus and preoptic area. Diazepam retarded or blocked amygdaloid kindling, and triggered a high frequency rhythm in the amygdala, hippocampus and preoptic area. Diazepam had no effect on any of the characteristics of the discharge or convulsion evoked by anterior neocortex stimulation even at twice the dose levels used for the amygdala group. Procaine and DPH blocked not only the convulsion but the AD as well. Eighty percent of the procaine and DPH treated rats failed to respond with neocortical AD even at 2,000 microamp current levels. Both procaine and DPH produced a weak but significant increase in the amplitude of the transcallosal evoked potential, while diazepam produced a weak decrement in that response. 26 references. (Author abstract modified)

218300 Bloom, Floyd E.; Landis, Story C. Lab. of Neuropharmacology, Div. of Special Mental Health Research, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Correlated histochemical, electron microscopical, pharmacological and physiological observation on aminergic mechanisms in the central nervous system. (Unpublished paper).** Washington, DC, NIMH, 1975. 14 p.

The structure and function of aminergic mechanisms in the central nervous system was investigated. Cytochemical, ultrastructural pharmacological and electrophysiological approaches were combined to study the effects of norepinephrine in the brain by comparing the actions of iontophoretically applied norepinephrine and related substances on neurons for which documentation of the presence of noradrenergic synapses can be adduced. Results have in general affirmed the descriptions of the noradrenergic innervation of the cerebellar cortex of the rat. The need for interdisciplinary cooperation in this type of research is stressed. 34 references.

218499 Rinaldi, P.; Sutko, M.; Mahnke, J. H.; Verzeano, M. Dept. of Psychobiology, Univ. of California, Irvine, CA 92664 **Serotonin in the lateral geniculate.** Physiology & Behavior. 14(1):95-102, 1975.

The action of serotonin in the lateral geniculate body of cats was examined. Serotonin was introduced in the lateral geniculate body of cats while the electrical activity at the point of injection was monitored with microelectrodes. Drug doses produced changes in the electrical activity characteristic of synchronization: increase in the rhythmicity and in the amplitude of the spontaneous gross waves and increase in the clustering of the spontaneous neuronal action potentials. The activity of the neurons which produced action potentials of high amplitudes was decreased, the activity of neurons which produced action potentials of low amplitudes was increased. Action potentials of different amplitudes were produced by neurons of different types. The synchronization of spontaneous activity seems of require the simultaneous excitation and inhibiton of two different types of neurons. In the lateral geniculate body, serotonin may be implicated in different ways in the different network structures responsible for the development of spontaneous as contrasted with evoked activity. 23 references. (Author abstract modified)

218957 Colon, E. J. Radboud Hospital, Department of Neurology, Nijmegen, the Netherlands **Long-lasting changes in**

cerebral neurons induced by drugs. Biological Psychiatry. 10(2):227-228, 1975.

The effect of d-amphetamine, haloperidol, and benzodi zepine on the cerebral cortical neurons was tested through determination of both the longitudinal and transverse axis of all neuronal nuclei in a circumscribed brain area 2 months after a 4 week period during which Wistar rats had received drugs. A long-lasting diminution was found in the nuclear volume after the use of d-amphetamine and haloperidol, while no changes in nuclear volume of cortical neurons could be detected after the use of benzodiazepine.

219111 Dubrovina, N. I.; Gilinskiy, M. A.; Il'yuchenok, R. Yu. Laboratoriya fiziologicheskikh mekhanizmov adaptivnogo povedeniya, Instituta fiziologii Sibirskogo filiala AMN SSSR, Novosibirsk, U.S.S.R. **/Comissural and sensory evoked potentials of the hippocampus following microiontophoresis of some drugs./** Komissural'nyy i sensornyy vyzvannyye potentsialy gippokampa pri mikroionoforeze nekotorykh veshchestv. Fiziologicheskiy zhurnal SSSR imeni I. M. Sechenova (Leningrad). 61(2):193-198, 1975.

The effects of sodium glutamate, gamma-aminobutyric acid (GABA), atropine and acetylcholine microiontophoresis on the focal responses evoked by stimulation of the forepaw and contralateral hippocampus were investigated in rats. No significant changes were observed in sensory potentials following drug application. Microiontophoresis of glutamate was found to produce changes in commissural responses. The positive wave was markedly depressed; the negative wave gradually increased in amplitude. GABA, atropine and acetylcholine all failed to evoke changes in commissural response; GABA, however, effectively blocked the effect of sodium glutamate. The ineffectiveness of atropine and acetylcholine microiontophoresis was tentatively attributed to the absence of cholinergic entries from the hippocampus and peripheries. 18 references. (Journal abstract modified)

219179 Smith, Thomas Lee. University of Nevada, Reno **Some neurochemical effects of N,N-dimethyltryptamine and their possible relation to acute schizophrenia. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-5312 HC$13.50 MF$5.00 92 p.

The effects of N,N-dimethyltryptamine (DMT), given either acutely or chronically for 1 month, on diencephalon norepinephrine (NE) and striatum dopamine (DA) neuronal systems in rat brain were studied. A pulse labeled technique was used to evaluate relative turnover rates of NE, DA, and their respective metabolites in control and drugged Ss. Via an alumination technique, catechols and their major metabolites were isolated from the same extract and fluorimetic analysis was performed to determine endogenous levels of the compounds. DMT given acutely or chronically enhanced the rate of DA synthesis. At 30 min after DMT injections, the level of DA's extraneuronal metabolite increased significantly. Thus it appeared that DA was released presynaptically at a faster rate than in controls. In chronic studies, NE and its extraneuronal metabolite normetanephrine exhibited a slight decrease in their synthesis rates, implying adrenergic adaptation. No significant change from controls was seen in the NE acute studies. Results suggest a causal connection between DMT, enhanced DA neurotransmission, and acute schizophrenia. (Journal abstract modified)

219288 Bloom, Alan S. University of Louisville **Interaction of cycloheximide and adrenergic drugs with brain protein and catecholamine biosynthesis. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-5460 HC$13.50 MF$5.00 97 p.

The effects of cycloheximide, diethyldithiocarbamate (DDC) and d-amphetamine on brain catecholamine levels and synthesis, and brain protein synthesis were examined in male C57B1/6j mice. Brain dopamine and norepinephrine levels were estimated using a modification of the fluorometric technique of Schellenberger and Gordon (1971). Catecholamine synthesis rates were estimated by measuring the conversion of H3-tyrosine to H3-dopamine and H3-norepinephrine. Brain protein synthesis was estimated by measuring the incorporation of H3-tyrosine into brain protein. Results suggest that cycloheximide produces an impairment of functional activity in catecholamine containing neurons which can be partially blocked by the administration of d-amphetamine. DDC also produces an impairment of the functional activity of catecholamine containing neurons, but this effect was not blocked by the amphetamine. DDC also inhibits protein synthesis. Findings of the behavioral and biochemical studies suggest the possibility that cycloheximide induced amnesia may be due at least in part to the impairment of functional activity in catecholamine containing neurons involved in memory formation. (Journal abstract modified)

219497 Mashkovskiy, M. D.; Andreyeva, N. I. Laboratoriya farmakologii, Vsesoyuznogo nauchno-issledovatel'skogo khimiko-farmatsevticheskogo instituta im. S. Ordzhonikidze, Moscow **/An experimental study of the psychotropic action of pyrazidol./** Eksperimental'noye izucheniye psikhotropnogo deystviya pirazidola. Farmakologiya i toksikologiya (Moskva). 38(1):5-10, 1975.

The pharmacological activity of pyrazidol was investigated in white mice. The influence of pyrazidol on the action of amphetamine, 5-hydroxytryptophan, epinephrine, norepinephrine, serotonin, reserpine and other neurotropic agents on body temperature and toxicity was recorded. The pharmacological action of 1,10-trimethylene-8-methyl-1,2,3,4-tetrahydropyrazino-1,2a-indole hydrochloride, i.e. pyrazidol, was found to closely approximate that of the tricyclic antidepressants. The distinctive features of pyrazidol included: absence of anticholinergic activity; presence of cataleptic effect; and low toxicity. Pyrazidol is concluded to be suitable for psychiatric use as an antidepressant. 15 references. (Journal abstract modified)

219498 Markin, V. A.; Mitrofanov, V. S. Laboratoriya farmakologii nervnoy sistemy, Instituta farmakologii AMN SSSR, Moscow **/A histochemical analysis of the influence of some psychotropic substances on the dehydrogenase activity of various brain structures./** Gistokhimicheskiy analiz vliyaniya nekotorykh psikhotropnykh veshchestv na degidrogenaznuyu aktivnost' razlichnykh struktur golovnogo mozga. Farmakologiya i toksikologiya (Moskva). 38(1):10-12, 1975.

The influence of triftazine, chlorpromazine, phthoracizine and lithium carbonate on the activity of flavine and nicotinamide adenine dinucleotide dependent dehydrogenases was investigated in rat brains. Histochemical analysis showed the psychotropic substances to exercise an elective effect on various structures and cellular elements of the limbic, corticoreticular and extrapyramidal systems. The specificity of action was found to depend upon the dose and period of administration: maximal changes occurred 3 hours after a single dose. Manifestations of adaptation to pharmacological action are noted in a number of cerebral formations in response to long-term drug administration. 8 references. (Journal abstract modified)

219499 Gusel', V. A. Leningradskogo pediatricheskogo meditsinskogo instituta, Leningrad **/The influence of cholinomimetics on the aftereffects of trace discharges and the activity of epileptogenic foci in the rabbit hippocampus./** Vliyaniye kholinomimetikov na sledovyye razryady posledeystviya i aktivnost' epileptogennogo ochaga v gippokampe krolikov. Farmakologiya i toksikologiya (Moskva). 38(1):13-15, 1975.

The effect of cholinomimetics on electrical activity of the hippocampus was investigated in rabbits with bipolar electrodes chronically implanted in cortical and subcortical structures. The introduction of arecoline and nicotine at the point of hippocampal stimulation with an electrical current was found to lower the threshold marking the development of aftereffect trace discharges. Cholinomimetics administered in the region of a penicillin induced epileptogenic focus in the hippocampus were found to suppress interictal epileptiform discharges apparent on the electroencephalogram (EEG). The cholinomimetics also suppresed epileptic seizures. High doses of cholinomimetics raised the thresholds of the aftereffect trace discharges and eliminated seizures in rabbits without affecting interictal epileptiform discharges on the EEG. 11 references. (Journal abstract modified)

219500 Tolpyshev, B. A. Chitinskogo meditsinkogo instituta, Chita, U.S.S.R. **/The effect of psychotropic agents on the electroencephalographic characteristics of the inhibitory function of the caudate nucelus./** Vliyaniye psikhotropnykh sredstve na elektroentsefalograficheskiye pokazateli tormoznoy funktsii khovostatogo yadra. Farmakologiya i toksikologiya (Moksva). 38(1):15-17, 1975.

The effects of psychotropic agents on the inhibitory function of the caudate nucelus were investigated in cats. Electroencephalogram (EEG) activity was measured by bipolar electrodes projected into the auditory and sensorimotor areas of the cortex. Chlorpromazine in doses of lmg/kg and haloperidol in doses of 0.5mg/kg were found to strengthen the inhibitory function elicited by low frequency stimulation of the caudate nucelus. Amphetamine and benactyzine eliminated and caffeine had no effect on caudate nucelus activity. 18 references. (Journal abstract modified)

219501 Losev, N. A.; Lapkin, V. A. Laboratoriya eksperimental'noy farmakoterapii otdela farmakologii, Instituta eksperimental'noy meditsiny AMN SSSR, Leningrad **/The influence of alkylate pherpacet derivatives on neuron populations in the midbrain reticular formation./** Vliyaniye fepratseta i ego alkilirovannykh proizvodnykh na neyronnyye populyatsii retikulyarnoy formatsii srednego mozga. Farmakologiya i toksikologiya (Moskva). 38(1):18-20, 1975.

The effect of microinjections of phenylisopropulamide of paraminophenylacetic acid derivatives on the excitability of neuron populations in the mesencephalic reticular formation of 48 rabbits was investigated. Changes in the functional condition of the mesencephalic reticular formation were determined by threshold magnitude and length of reaction activation in response to electrical stimulation. Pherpacet was found to exert a beta-adrenolytic action; the propylic analog exerted an alpha-adrenolytic central action; the methyl and ethyl analogs blocked both types of receptors. No changes were found in the vegetative functions of the organism. 7 references. (Journal abstract modified)

219504 Ryzhenkov, V. Ye.; Khechinashvili, G. G. Otdel farmakologii, Insituta eksperimental'noy meditsiny AMN SSSR, Leningrad **/The effect of 6-hydroxydopamine and reserpine on the mobilization of carbohydrates and fats in stimulated rats./** Vliyaniye 6-gidroksidofamina i rezerpina na mobilizatsiyu uglevodov i zhirov pri razdrazhenii krys. Farmakologiya i toksikologiya (Moskva). 38(1):25-29, 1975.

The effect of antiadrenergic substances on the role of the sympathetic nervous system in the mobilization of carbohydrates and fats was investigated in stimulated rats. The administration of 6-hydroxydopamine was found to inhibit basal lipolysis, but did not hinder the development of adipokinetic and hyperglycemic reactions in response to stimulation. In rats with depressed sympathetic adrenal systems, the rate of rising concentration of free fatty acids in the plasma in response to stimulation caused the development of hypoglycemia. Reserpine did not hamper lipolysis, and it lessened the degree of the hyperglycemic reaction to stimulation. 30 references. (Journal abstract modified)

219505 Liberman, S. S.; Sharova, S. A. Vsesoyuznogo nauchno-issledovatel'nogo khimiko farmatsevticheskogo instituta im. Ordzhonikidze, Moscow **/A comparison of the action of the tricyclic antidepressants, azaphen and imipramine, on the gastrointestinal tract of test animals./** Sraveniye deystviya trisiklicheskikh antidepressantov azafena i imizina na zheludochno-kishechnyy trakt eksperimental'nykh zhivotnykh. Farmakologiya i toksikologiya (Moskva). 38(1):29-32, 1975.

The effect of azaphen and imipramine on the gastrointestinal tract was investigated in mice and rats. Gastrointestinal tract activity was measured by secretions within the tract as well as by excretory functions. Both single and repeated introduction of azaphen was found to have no effect upon the normal activity of the gastro intestinal tract, nor did it significantly affect the function of the liver. Imipramine, however, was found to inhibit the secretion of the salivary and gastric glands, to hinder the motoricity, to reduce the excretory capacity of the gastrointesntinal tract and to cause damage to the hepatic function. The effects of imipramine are tentatively concluded to be caused by its cholinolytic properties. 7 references. (Journal abstract modified)

219506 Zavodskaya, I. S.; Moreva, E. V.; Zaskal'ko, N. I.; Bul'on, V. V. Laboratoriya eksperimental'noy farmakologii, Instituta eksperimental'noy meditsiny AMN SSSR, Leningrad **/The effect of catecholamines on the norepinephrine level in the tissues./** Vliyaniye katekholaminov na soderzhaniye noradrenalina v tkanyakh. Farmakologiya i toksikologiya (Moskva). 38(1):44-46, 1975.

The effect of catecholamines on the norepinephrine level in the tissues was investigated in rabbits and rats. Intravenous administration of toxic doses of catecholamines was found to produce a rise of the norepinephrine level in the heart and the aorta. However, intramuscular or intraperitoneal administration of catecholamines caused the norepinephrine content to decrease. 11 references. (Journal abstract modified)

219507 Terekhova, N. M. Kafedra farmakologiya Permskogo meditsinskogo instituta. **/Towards the mechanism of the antiphlogistic action of chlorpromazine./** K mekhanizmu protivovospalitel'nogo deystviya aminazina. Farmakologiya i toksikologiya (Moskva). 78(1):55-57, 1975.

The antiinflammatory action of chlorpromazine was investigated in rats and rabbits. Chlorpromazine (3.5or 1mg/kg) produced an antiphlogistic effect in an aseptic inflammation induced by introduction of formalin, serotonin, histamine, agar, dextran and bradykinin. These doses also lowered the permeability of the vessels to an I131-labeled albumin. In doses of 5 mg/kg chlorpromazine lowered the activity of kinins and

hyaluronidase and suppressed the proliferative processes of the connective tissue around a foreign body. 8 references. (Journal abstract modified)

219508 Kuznetsova, N. A. Bashkirskogo meditsinskogo instituta, Ufa, U.S.S.R. **/The specificity of action exerted by neurotropic agents during sensitization./** Ob osobennostyakh deystviya nekotroykh neyrotropnykh sredstv pri sensibilizatsii. Farmakologiya i toksikologiya (Moskva). 38(1):62-63, 1975.

The effect of neurotropic agents on albino mice was investigated following sensitization. The sensitivity of the mice to the hypothermic action of chlorpromazine and reserpine was found to diminish, while sensitivity to imipramine increased. Sensitivity to hexobarbital sodium, barbital sodium and chloralhydrate were found to increase in tests involving the duration of sleep elicited by these drugs. Sensitivity to the central action of arecoline and to the toxicity of chlorpromazine increased. (Journal abstract modified)

219522 Fernando, J. C.; Joseph, M. H.; Curzon, G. Institute of Neurology, Queen Square, London WC1N 3BG **Tryptophan plus a pyrrolase inhibitor for depression?** Lancet (London). No. 7899:171, 1975.

The effects of all opurinol plus tryptophan and nicotinamide plus tryptophan on rat brain tryptophan are cited to indicate that allopurinol could increase the availability of a tryptophan load to the brain. The evidence does not support the hypothesis that nicotinic acid derivatives have similar effects. However, it is noted that this might occur in certain circumstances, such as after feeding, when the two actions of nicotinic acid tending to decrease tryptophan availability, the antilipolytic and pyrrolase inducing effects, both become less important so that pyrrolase inhibition may then dominate. 6 references.

219606 Nemtsov, A. V.; Dubinskaya, G. R. Otdel psikhofarmakologii, Moskovskogo nauchno-issledovatel'skogo instituta psikhiatrii Ministerstva zdravookhraneniya RSFSR, Moscow **/The effect of neuroleptics of the phenothiazine series on pulse activity and the ultrastructure of rabbit cortical neurons./** Vliyaniye neyroleptikov fenotiazinovogo ryada na impul'snuyu aktivnost' i ul'trastrukturu korkovykh neyronov krolika. Byulleten' eksperimental'noy biologii i meditsiny (Moskva). 79(4):64-68, 1975.

The influence of phenothiazine neuroleptics on pulse activity and on the ultrastructure of cortical neurons was investigated in rabbits to determine the integration of ultrastructural changes. Chlorpromazine injections were found to produce the following effects: disaggregation of polysomes; dilation of endoplasmic reticulum cisternae; hypertrophy of the golgi apparatus; swelling of the mitochondria in the majority of the cortical neurons. Inhibition of pulse activity of the nerve cells corresponded to these ultrastructural changes. Triphthazine caused a thickening of the matrix of a part of the neurons and an increase in pulse activity of that group of cortical cells under triphthazine influence. It was concluded that differences in changes in pulse activity and neuron ultrastructure are based on the differences in the spectrum of the psychotropic activity of the neuroleptic - phenothiazine derivatives. 13 references. (Journal abstract modified)

219633 Ondo, Jerome G. Dept. of Physiology, Medical University of South Carolina, 80 Barre St., Charleston, SC 29401 **Neurotransmitters affecting pituitary hormone release. (Unpublished paper).** Final Report, NIMH Grant MH-25408, 1975, 2 p.

The effects of certain amino acids on the control of pituitary gonadotropin and prolactin secretion were studied. Gamma-aminobutyric acid (GABA) injected into the third ventricle of pentobarbital anesthetized male rats promoted the release of pituitary luteinizing hormone (LH) and prolactin but not follicle stimulation hormone. Doses of either 2 or 8 micromoles GABA promoted hormone secretion. When GABA was injected directly into the anterior pituitary it was ineffective in altering plasma levels of either LH or prolactin. Two micromoles of glycine elevated prolactin, while 2.0micromoles of glutamate of lysine had no effect. Intrapituitary injections of glycine were also incapable of promoting prolactin release. Evidence suggests that GABA and other amino acids may play a role in the regulation of pituitary LH and prolactin secretion by controlling the discharge of hypothalamic neurohormones. 2 references. (Author abstract modified)

219663 Buznikov, G. A.; Manukhin, B. N.; Rakich, L.; Aroyan, A. A.; Kucherova, N. F.; Suvorov, N. N. Laboratoriya fiziologii im. Koshtoyantsa, Instituta biologii razvitiya AN SSSR, Moscow **/On the mechanism of the defensive action of acetylcholine and serotonin against their cytotoxic antagonists./** O mekhanizme zashchitnogo deystviya atsetilkholina i serotonina protiv ikh tsitotoksicheskikh antagonistor. Zhurnal evolyutsinnoy biokhimii i fiziologii (Leningrad). 11(2):128-133, 1975.

The protective mechanism of acetylcholine and serotonin against their own cytotoxic antagonists was investigated in sea urchin (Arbacia lixula) embryos, incubated in solutions of cytotoxic cholinolytics and serotoninolytics. During the first rapid stage of binding, the embryos accumulated a level of serotoninolytics which was two to six times higher than the external concentration; during the second stage of binding, the level increased to 8-12 times the external concentration. The protecting action of exogenous acetylcholine and serotonin against their cytotoxic antagonists did not inhibit their accumulation in embryonic cells. The protecting action was, therefore, attributed to the decrease in the sensitivity of embryos to neurophysiological drugs. The protecting effect of the endogenous factor produced by eggs and embryos was concluded to be associated with the inhibition or abolition of the second stage of binding of cytotoxic neuropharmacological drugs. 14 references. (Journal abstract modified)

219709 Guilland, J. C.; Klepping, J.; Escousse, A.; Didier, J. P.; Rucart, G.; Mounie, J. Laboratoire de Physiologie, Faculte de Medecine de Dijon, 7, boulevard Jeanne-d'Arc, 21033 Dijon Cedex, France **/Experimental investigation of a new amphetamine derivative./** Etude experimentale d'un nouveau derive de l'amphetamine. Therapie (Paris). 30(1):117-124, 1975.

The effect of a new amphetamine derivative, S-992 (meta-trifluoro-methyl-phenyl)-1-(beta-(benzoyl-oxy) ethyl)-amino-2-propane chlorhydrate), on free plasma fatty acid rates, plasma triglyceride rates, and adipocyte cellularity was investigated in the rat. Treatment of rats for 8 days with an oral dose of 50mg/kg of S-992 caused the following changes in all animals: a decrease in alimentary ingestion which was only significant during the first days of treatment; a decrease in weight which remained significant 8 days after beginning treatment; no significant modification of free fatty acids and plasma triglycerides in blood samples taken 5 hours after ingestion of the last dose of S-992; a significant decrease in the size of adipose cells. It is concluded that this substance plays a role of reducing adipose reserves rather than being a true anorexigene. 11 references.

219747 Dvorkin, V. Ya; Kiselev, G. V.; Chetverikov, D. A. no address /**The metabolism of individual phospholipid fractions in the rat brain during thiopental sleep and amphetamine excitation.**/ Obmen otdel'nykh fraktsiy fosfolipidov v golovnom mozge krys pri tiopentalovom sne i fenaminovom vozbuzhdenii. Byulleten' eksperimental'noy biologii i meditsiny (Moskva). 79(2):40-42, 1975.

The dependence of phospholipid metabolism on the functional activity of the central nervous system was investigated in white Wistar rats. Phospholipid fractions in the rat brain were found to decrease markedly during thiopental induced sleep, and to increase markedly during amphetamine excitation. The content of diphosphoinositide rose by 39% during thiopental induced sleep and diminished during amphetamine excitation. No changes occurred in the content of other phospholipid fractions. Polyphosphoinositide metabolism was concluded to be connected with the brain energetic processes, and to be only nominally related to the level of the central nervous system functional activity. 5 references. (Journal abstract modified)

219749 Saratikov, A. S.; Spiridonova, Z. I.; Alekseyeva, L. P. Tomskogo meditsinskogo instituta, Tomsk, U.S.S.R. /**The effect of lithium on the content of catecholamines in the brain of rabbits and rats.**/ Vliyaniye litiya na soderzhaniye katekholaminov v mozge krolikov i krys. Byulleten' eksperimental'noy biologii i meditsiny (Moskva). 79(2):55-57, 1975.

The effect of lithium chloride on the level of catecholamines and dioxyphenylalanine was investigated in various areas of the brains of rabbits and rats. Lithium chloride injections of 200 mg/kg failed to significantly alter the level of catecholamines and dioxyphenylalanine in the rat brainstem. Intravenous lithium chloride injections in doses of 100mg/kg increased the noradrenaline concentration in the thalamus, hypothalamus, reticular formation and caudate nucleus of the rabbit brain. The increased noradrenaline concentration was accompanied by an increase in dopamine content in the caudate nucleus with a simultaneous reduction of its concentration in the thalamus, hypothalamus, reticular formation, amygdala and the hippocampus. It is concluded that the adrenergic and dopaminergic processes participate in the mechanism of the psychotropic effect of lithium. 16 references. (Journal abstract modified)

220312 Teitelbaum, Herman; Lee, Jack F.; Johannessen, Jan N. Armed Forces Radiobiology Research Institute, Defense Nuclear Agency, Bethesda, MD 20014 **Behaviorally evoked hippocampal theta waves: a cholinergic response.** Science. 188(4193):1114-1116, 1975.

The responses of the hippocampus to forced running and to physostigmine, the reaction of both to scopolamine (a known cholinergic blocking agent), and the effect of septal lesions on both responses, were investigated in 30 male Sprague-Dawley rats. Forced running in a treadmill resulted in the instantaneous electroencephalographic pattern in the dorsal hippocampus of the rat. A similar bioelectric response in the absence of movement was induced by physostigmine. Both responses were blocked with scopolamine. Lesions of the medial septal nucleus abolished hippocampal theta waves induced by forced running or physostigmine. 11 references. (Author abstract modified)

220314 Brown, Ian R.; Liew, C. C. Department of Zoology, Scarborough College, University of Toronto, West Hill, Ontario, Canada **Lysergic acid diethylamide: effect on histone acetylation in rabbit brain.** Science. 188(4193):1122-1123, 1975.

The effect of d-lysergic acid diethylamide (LSD) on the acetylation of histones in various regions of the rabbit brain was investigated. Results indicate that lysergic acid diethylamide increased acetylation of histones in rabbit cerebral hemispheres and midbrain 30 minutes after intravenous administration of the drug at doses of 10 and 100 micrograms per kilogram of bodyweight. Evidence for the stimulation of acetylation in individual histone bands was obtained after separation by electrophoresis on polyacrylamide gels. 12 references. (Author abstract modified)

220472 Choi, R. Leslie. University of California **The distribution kinetics and turnover of choline and acetylcholine in plasma and brain of rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-9385 HC$13.50 MF$5.00 183 p.

The distribution kinetics of plasma and brain choline (Ch) and of brain acetylcholine (Ach) were studied in rats to elucidate the mechanisms by which cholinergic neurons function in the brain. The possible existence of isotope effects involving the isotopic variants was examined on various in vitro preparations representing enzymes and receptors of the cholinergic nervous system, as well as the effects of HC-3 on brain Ch and ACh. Findings indicate that: (1) endogenous plasma Ch turnover rate was fairly rapid and constant despite increases in the total Ch level during infusion of labelled Ch at various rates; (2) the uptake of Ch from plasma to brain was proportional to the plasma Ch level, and the rate of uptake from plasma to brain was slow compared to the turnover of Ch within the brain; (3) AcH turnover rate varied between regions. (Journal abstract modified)

220475 Mehta, Chander Shivlal. Washington State University **Possible role of adenosine-3',5'-monophosphate and biogenic amines in morphine and cocaine treated rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-7658 HC$13.50 MF$5.00 97 p.

Effects of chronic morphine and cocaine administration and of morphine tolerance and withdrawal were studied with respect to alterations in the endogenous brain concentrations of norepinephrine, serotonin, dopamine and adenosine-3',5'-monophosphate (cyclic AMP) of male Sprague-Dawley rats. Drug induced tranquilization, sedation and myoneural blockade were used to assess the influence of convulsions precipitated by sacrifice with microwave irradiation upon brain levels of cyclic AMP. The endogenous levels of cyclic AMP declined significantly after pretreatment with prochlorperazine ethanedisulfonate, morphine, sodium phenobarbital, sodium seconal, chloral hydrate, and d-tubocurarine chloride. In morphine pellet implantation experiments, the endogenous brain cyclic AMP levels were maximum in Ss implanted subcutaneously with pellets in the dorsal cervical region for 3 days and subsequently challenged with the morphine antagonist, naloxone hydrochloride. A decline in the levels occurred if pellets were left in the body for 3 days. In chronically morphinized Ss undergoing naloxone hydrochloride withdrawal, the cerebellar cyclic AMP was significantly higher than controls. Chronic cocaine hydrochloride administration caused a decrease in cerebellar catecholamines and striatal dopamine. (Journal abstract modified)

220904 Maruyama, Shoji; Kawasaki, Tadashi. Department of Neurophysiology, Brain Research Institute, Niigata University, Niigata, Japan **Synergism between gamma-aminobutyric acid and butyrophenones administered microelectrophoretically in the Purkinje cells of the cat cerebellum.** Japanese Journal of Pharmacology (Kyoto). 25(2):209-213, 1975.

The interaction between gamma-aminobutyric acid (GABA) and butyrophenones administered microelectrophoretically was investigated by observation of their effects on the activities of Purkinje cells in the cat cerebellum. In 26 of 30 cells GABA completely or significantly inhibited the l-glutamate induced firing; in 2 cells it depressed the firing slightly; in 2 cells it produced no clear depression. In 22 of 30 cells droperidol inhibited the firing to some extent; in 8 cells it did not depress the firing. When applied with ejecting currents of 80 or 100 nA, chlorpromazine, a neuroleptic of the phenothiazine type, did not produce any depressant effect on the spontaneous firing in all of 9 Purkinje cells. The results indicate that when applied microelectrophoretically, droperidol produces the depressant action on the spontaneous or glutamate induced firing of Purkinje cells and also enhances the depressant effect of concurrently administered GABA on the spontaneous firing of Purkinje cells. Either direct action on GABA receptors or inhibition of a specific uptake process for GABA, or both, at GABA operated synapses is implicated in a fundamental mechanism of the action of butyrophenones. The results suggest that unlike butyrophenones, phenothiazines do not act on the postsynaptic membrane of GABA operated synapses. 18 references.

220944 LaManna, Joseph C.; Rosenthal, Myron. Department of Physiology and Pharmacology, Duke University Medical School, Durham, NC 27710 **Effect of ouabain and phenobarbital on oxidative metabolic activity associated with spreading cortical depression in cats.** Brain Research (Amsterdam). 88(1):145-149, 1975.

The effects of small intracortical injections of ouabain and of systemically administered phenobarbital on the fluorescence changes that occur due to the production of spreading depression (SD) were examined in the cat. Spreading depression was produced by suprathreshold intensities of direct cortical stimulation, usually 1 sec trains of 20 Hz pulses of 0.5msec duration. Stimulation intensities were kept constant through the experiment. Increasing ouabain doses slowed the decrease in the metabolic signal during SD. The drug, had no effect on the subsequent rate of recovery of this signal to baseline levels. In fact, ouabain had three apparent effects on the opitcal signal. The drug also decreases the signal amplitude and finally, it was consistently observed that after ouabain administration the decrease of fluorescence becomes more complex and a plateau effect is apparent. This effect is more obvious in a 1 mm diameter field although the retardation of on kinetics is also seen in a 3.2mm field. Phenobarbital had no effect on 'on' kinetics.

220945 Drucker-Colin, Rene Raul; Giacobini, Ezio. Department de Biologia Experimental, Instituto de Biologia, UNAM, Apartado Postal 70-600, Mexico 20, D. F., Mexico **Sleep-inducing effect of piperidine.** Brain Research (Amsterdam). 88(1):185-189, 1975.

The behavioral and electophysiological manifestations following perfusion of piperidine with a push pull cannula system into a defined areas of the brainstem of the cat were examined. The intracerebral injection of piperidine in the midbrain reticular formation (MRF) produced a selective and powerful hypnogenic effect in the cat. That slow wave sleep (SWS) duration was not significantly increased may merely reflect the fact that SWS usually represents about 75% of total sleeping time. This, in addition to the fact that recordings lasted only 60 min, may have precluded a significant change in the duration of SWS. Rapid eye movement sleep was much more labile, thus even a small change was detected. The finding of a powerful and local pharmacological action of piperidine favors the hypothesis of a physicological stimulation or modulation of cholinergic hypnogenic structures of the MRF, providing that the piperidine would be localized in nerve cells, and released from a specific area of the brainstem during sleep. The present evidence for this hypothesis is supported by the physiological presence of piperidine in the brain of vertebrates and invertebrates, its physiological accumulation in the brain of dormant invertebrates and vertebrates, and its topic pharmacological action. 19 references.

220947 Elazar, Z.; Gottesfeld, Zehava. Department of Physiology and Pharmacology, Tel Aviv University Sackler School of Medicine, Tel Aviv, Israel **Effect of drug-induced increase of brain GABA levels on penicillin focus** Experientia (Basel). 31(6):676-678, 1975.

The inhibitory effect of gamma-aminobutyric acid (GABA) on penicillin induced seizures was examined in cats and rats. The endogenous concentrations of GABA in the brain were elevated by the administration of aminooxyacetic acid (AOAA) and di-n-propylacetate (DPA). Administration of AOAA resulted in elevated GABA concentration in cat cerebral cortex by 41% compared to control, whereas in the penicillin focus GABA was decreased. It appears that the decrease of GABA in the spiking focus cannot be prevented by the treatment of AOAA. A second series of experiments was designed to test whether a greatly increased GABA level, caused by 30mg/kg of AOAA, would inhibit the appearance of seizures in the focus. Penicillin was applied 5 h after AOAA injection and interictal spikes appeared, as usual, minutes later, followed by seizure activity 30 min thereafter. Thus, the increased GABA did not prevent the development of seizure in the focus cortex in rats. Seizures activity before and 60 min after DPA administration remained essentially unchanged and continued to be long lasting. It is concluded that increased GABA after AOAA or DPA has no, or a very weak, antiepileptic on pencillin spiking foci. 19references.

220948 Koe, B. K. Dept. of Pharmacology, Pfizer Inc., Eastern Point Road, Groton, CT 06340 **Monoamine oxidase inhibitors antagonize the acceleration of brain dopamine synthesis induced by neuroleptic drugs in vivo: implications for the treatment of tardive dyskinesia.** Experientia (Basel). 31(6):669-671, 1975.

The effect of monoamine oxidase (MAO) inhibitors on the acceleration of brain dopamine (DA) synthesis induced by neuroleptic drugs was examined in the corpus striatum of the rat in vivo. Administration of trifluoperazine or tetrabenazine followed by the decarboxylase inhibitor elicited dopa accumulations three to four times that found in control rats receiving NSD-1024 (3-hydroxy-O-bentylhydroxylamine hydrochloride). Pargyline, MAO inhibitor, itself reduced dopa accumulation. Combining pargyline with trifluoperazine gave less dopa accumulation than that shown by control rats whereas pargyline in combination with tetrabenazine virtually halted dopa formation. Antagonism of the accelerated synthesis of DA elicited by the neuroleptic drugs increased with the pargyline dose. The MAO inhibitor pheniprazine also blocked the acceleration of DA synthesis. The increase in DA levels after the MAO inhibitors was consistent with the decrease in MAO activity of brain homogenates. It is suggested that free DA is available after treatment with MAO inhibitor plus tetrabenazine, thereby resulting in greater inhibition of tyrosine hydroxylase and cut back in dopamine synthesis. 20 references.

220949 Hamberger, B.; Tuck, J. R. Department of Histology, Karolinska Institutet, S-104 01 Stockholm, Sweden **3H-nortriptyline uptake and tissue-binding in vitro and its effect on 3H-noradrenaline uptake.** Experientia (Basel). 31(6):667-668, 1975.

3H-nortriptyline (NT) uptake and tissue binding and its effect on 3H-noradrenaline (NA) uptake were explored in the rat in vitro. 3H-NT accumulates rapidly in brain slices during incubation in buffer. After 2 h, a more than 100 fold accumulation of radioactivity appeared in the slices as compared to the medium. It is suggested that accumulation of 3H-NT in contrast to 3H-NA accumulation is nonspecific and not energy dependent. The rapid accumulation of NT is most likely related to its high lipid solubility. Methodological considerations in in-vitro experiments of drug binding to tissue components and plasma proteins are discussed, as well as clinical implications for the use of tricyclic antidepressants. 9 references.

220972 Roth, Jerome A. Department of Anesthesiology, Yale University School of Medicine, New Haven, CT 06510 **Inhibition of rabbit monoamine oxidase by doxepin and related drugs.** Life Sciences. 16(8):1309-1319, 1975.

The inhibition of both B and A forms of rabbit lung mitochondrial monoamine oxidase (MAO) by doxepin is reported. It is concluded that doxepin is similar to other tricyclic antidepressant drugs in that it has a greater affinity for the B form of the rabbit oxidase. The ability of doxepin and imipramine and its mono and didesmethyl derivations to inhibit rabbit MAO is decreased as the pH is raised above 8.0. Results suggest that the basicity of the propylamine side chain has little or no influence on the ability of these drugs to inhibit the rabbit oxidase. These results support the hypothesis that affective disorders are associated with a change in the type B form of human MAO; the relationship between this form of the oxidase and catecholamine theory of affective disorders, however, remains obscure. 14 references. (Author abstract modified)

220974 Gudelsky, Gary A.; Thornburg, John E.; Moore, Kenneth E. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **Blockade of alpha-methyltyrosine-induced supersensitivity to apomorphine by chronic administration of L-dopa.** Life Sciences (Oxford). 16(8):1331-1338, 1975.

The blockage of alpha-methyltyrosine induced supersensitivity to apomorphine by chronic administration of L-dopa is reported in mice. The locomotor stimulating effect of apomorphine was enhanced in mice maintained for 2 weeks on a diet containing alpha-methyltyrosine suggesting that chronic blockade of catecholamine synthesis increases the sensitivity of central dopaminergic receptors. Concurrent administration of L-dopa with alpha-methyltyrosine effectively restored the alpha-methyltyrosine depleted brain catecholamine stores and prevented the enhancement of the response to apomorphine. These data support the concept that the development of alpha-methyltyrosine induced supersensitive dopaminergic receptors in the brain results from a chronic deficiency of dopamine at these receptors. 23 references. (Author abstract)

220975 Dafny, N. Neurobiology, University of Texas Medical School, Houston, TX 77025 **Effects of reserpine and L-dopa in the globus pallidus of freely behaving rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 215(1):31-39, 1975.

Paired click stimuli applied at varying time intervals were used to study the responses to polysynaptic input in the globus pallidus of freely behaving rats chronically implanted with semimicroelectrodes. The average acoustic evoked responses (AAER) to 32 successive acoustic stimuli consisted of large amplitude potentials of long duration composed of five components with long latencies. The neuronal recovery function was long. Intraperitoneal reserpine administration heightened the amplitude of the AAER and shortened the neuronal recovery function. L-DOPA injection 2 hr after reserpine treatment caused further heightening of the AAER but had no effect on the neuronal recovery function. When L-DOPA was given first, the AAER increased in the amplitude response and the neuronal recovery function was shortened consistently. Reserpine treatment 2 hr after L-DOPA, decreased the amplitude of the AAER but had no marked effect on the neuronal recovery function. 20 references. (Author abstract)

220976 Van Zwieten, P. A. Dept. of Pharmacy, University of Amsterdam, Plantage Muidergracht 24, Amsterdam, The Netherlands **A benzodioxanhydroxyethylpiperidine derivative with acute central hypotensive action, different from that of clonidine: a comparison with neuroleptic agents.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 215(1):104-118, 1975.

(Author abstract) Erythro-1-(1-(2-(1,4-benzodioxan-2-yl)-2-OH-Et)-4-piperidyl)-2-benzimi azolinone (R 28935), a new benzodioxanhydroxyethylpiperidyl derivative which proved to possess potent central hypotensive activity when injected into the left vertebral artery of anaesthetized cats was examined. Although almost as potent as clonidine, its hypotensive action is more prolonged. The central hypotensive effect is dose dependent and stereospecific, the threo isomer being much less effective than the erythro form. In contrast to the effect of clonidine, the centrally induced hypotensive action of R 28935 is not diminished after pretreatment with piperoxane, yohimbine or desipramine; central alpha-adrenergic receptors are probably not involved in the central hypotensive action of R 28935. The following surgical interventions did not diminish the central hypotensive action of R 28935: bilateral vagotomy, bilateral cervical sympathectomy, bilateral extirpation of the stellate ganglia. It is concluded that R 28935 depresses peripheral sympathetic tone via a centrally induced primary effect. 23 references. (Author abstract modified)

220977 Lindenbaum, A.; Marcher, K.; Wepierre, J.; Cohen, Y. Laboratoire de Pharmacodynamie, Rue Jean Baptists Clement, 99290 Chatenay - Malabry, France /**The blood-brain barrier II: distribution kinetics of 3H parahydroxyamphetamine in brain structures of the rat after intravenous administration.** Barriere hemato-encephalique II: cinetique de distribution de la parahydroxyamphetamine 3H dans le structures du cerveau de rat apres administration intraveineuse. Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 215(1):168-176, 1975.

The distribution of para-hydroxyamphetamine in the brain of rats was examined after intravenous administration. Intravenously injected parahydroxyamphetamine hardly penetrates into the central nervous system, since, 5 minutes after injection, the tissue to plasma concentration ratio for brain and cerebrospinal fluid amounts to 0.67 and 0.35 respectively. Its concentration in muscle is five times higher than in plasma. In the brain, the molecule is preferentially taken up by the corpus striatum and the hypothalamus. Thus, parahydroxylation of amphetamine inhibits the penetration of the molecule into the brain and suppresses its cortical fixation. These characteristics could explain why this parahydroxylated amine has no psychotropic action. 17 references. (Author abstract)

221030 Stephens, D. N.; Herberg, L. J. Institute of Neurology, Queen Square, London WC1N 3BG **Catecholamines and self-stimulation: pharmacological differences between near- and far-lateral hypothalamic sites.** Brain Research (Amsterdam). 90(2):348-351, 1975.

The pharmacological differences between near and far lateral hypothalamic sites were examined in the rat in relation to catecholamines and self-stimulation. In the group as constituted, both D-amphetamine and L-amphetamine produced a significant enhancement of self-stimulation in the hour following injection, but the D-isomer was significantly more potent. This result supports the suggestion that hypothalamic self-stimulation is preponderantly noradrenergic but analysis of individual scores revealed differentials ranging from less than zero to more than 100, and at least seven of the implants were located at the predominantly dopaminergic end of the scale. Data indicate that the most laterally placed electrodes were those which had been classified as dopaminergic. 16 references.

221031 Mao, C. C.; Guidotti, A.; Landis, S. Laboratories of Preclinical Pharmacology, National Institute of Mental Health, St. Elizabeths Hospital, Washington, D.C. 20032 **Cyclic GMP: reduction of cerebellar concentrations in 'nervous' mutant mice.** Brain Research (Amsterdam). 90(2):335-339, 1975.

In a study of the role of 3',5'-cyclic-guanosine monophosphate (cGMP) in the mechanisms of cerebellar neurotransmission, the association between particular cerebellar cell types and changes in cyclic necleotide levels was examined. The cerebellar cGMP concentration of nervous mutuant mice of both genetic backgrounds was decreased by about 50% and 70% in the outcrossed and the Balb/cGR mice, respectively. No significant change in cAMP concentration was found. Diazepam was, ineffective in changing the cerebellar concentration of cGMP in nervous mutant mice even though the normal reduction of cGMP was obtained in the cerebellum of littermate animals. Injection of the drug appeared to reduce the exploratory behavior of normal littermate mice but this effect was less obvious in the mutant mice. As previously observed, diazepam did not affect cAMP concentrations in normal mice nor did it affect the level of the nucleotide in the mutant mice. The results show that in nervous mutant mice in which only 10% of the Purkinje cells are present and presumably functional, there is a marked reduction in the cGMP concentration of the cerebellum without any significant change in cAMP concentration. 22 references.

221032 Oliverio, Alberto; Castellano, Claudio; Renzi, Paolo. Laboratorio di Psicobiologia e Psicofamacologia, C. N. R., Via Reno 1, Rome 00198, Italy **Genotype or prenatal drug experience affect brain maturation in the mouse.** Brain Research (Amsterdam). 90(2):357-360, 1975.

The patterns of postnatal development of electrocortical activity were examined in C57BL/6J (C57) and SEC/1ReJ (SEC) male and female mice. Since maternal chronic drug experience has been shown to affect offspring behavior, the effects of in utero administration of amphetamine on development of electrocortical activity were also studied. It was found that there is a progressive maturation of the spontaneous electrocorticogram (ECoG) which reaches an adult level of development after the 12th day after birth. It was also found that development of a regular rhythmic and high voltage ECoG occurs at an earlier age in the offspring of amphetamine treated mothers than in control mice. The results indicate that species which are behaviorally mature at birth also show an adult like ECoG activity while in species immature at birth, such as primates or man, there is a long lasting postnatal maturation. It is felt that the fact that in utero administration of low doses of amphetamine modifies cortical development should be considered in relation to its possible implications for man. 13 references.

221037 Oliverio, Alberto; Castellano, Claudio; Eleftheriou, Basil E. Laboratorio di Psicobiologia e Psicofarmacologia, C.N.R., Rome **Morphine sensitivity and tolerance: a genetic investigation in the mouse.** Psychopharmacologia (Berlin). 42(3):219-224, 1975.

Sensitivity and tolerance to morphine were determined in two strains of mice, BALB/cBy and C57BL/6By, their reciprocal F1 hybrids and seven of their recombinant inbred strains. Sensitivity was established based on locomotor activity following the administration of saline, 10 or 20mg/kg of morphine hydrochloride, while tolerance was established according to the hot plate method following the single or repeated administration of saline, 5, 10, or 20mg/kg of morphine hydrochloride. Results indicate that both sensitivity and tolerance to morphine are genotype dependent and their inheritance is characterized by dominance or partial dominance. Further clarification of the genetic relationship of sensitivity, tolerance and analgesia to morphine must await analysis of the brain morphine binding protein currently being conducted. 21 references. (Author abstract)

221038 Kushinsky, K. Department of Biochemical Pharmacology, Max Planck Institute for Experimental Medicine, D-3400, Gottingen, Germany **Does chronic morphine treatment induce a supersensitivity of dopamine receptors in rat brain?** Psychopharmacologia (Berlin). 42(3):225-229, 1975.

In order to determine whether chronic morphine treatment increases the sensitivity of dopamine receptors in rat brain, the effectiveness of apomorphine in inducing stereotyped behavior and decreasing the dopamine turnover in the striata was examined. Acute morphine treatment slightly reduced stereotyped behavior induced by L-Dopa and by apomorphine. In morphine withdrawn rats, apomorphine was no more effective than saline in inducing stereotypies (sniffing, licking, gnawing). However, the ability of apomorphine to lower striatal dopamine turnover was increased in morphine withdrawn rats. Despite these latter observations, chronic morphine treatment probably did not induce a supersensitivity of dopamine receptors in rat brain. 20 references. (Author abstract)

221042 Shuster, L.; Webster, G. W.; Yu, G.; Eleftheriou, B. E. Department of Biochemistry and Pharmacology, Tufts University School of Medicine, Boston, MA **A genetic analysis of the response to morphine in mice: analgesia and running.** Psychopharmacologia (Berlin). 42(3):249-254, 1975.

Two progenitor strains, BALB/cBy and C57BL/6By, their reciprocal F1 hybrids, and seven of their recombinant inbred derived lines were used to examine the genetic basis of the response to thermal pain, and morphine analgesia at doses of 2.5, 5.0and 10.0mg/kg. Both the latency of response to thermal pain and the analgesic response differed significantly among the various strains tested. Strong genetic determinants appear to control their responses. Analyses of the data did not permit clarification regarding the linkage of these determinants. Photoelectric activity cages were used to test the running response of the same strains to 12.5, 25 and 40mg/kg morphine sulfate. The genetic determinants for running activity were different from those for analgesia. There is evidence for two or more loci controlling the behavior at 60 and 75 min after injec-

tion, but not enough information to define the loci involved. 19 references. (Author abstract)

221051 Sitaramam, V.; Ramasarma, T. Department of Biochemistry, Indian Institute of Science, Bangalore, India 560 012 **Inhibitory action of norepinephrine on the induction of tryptophan-2,3-dioxygenase by cortisol: mediation by the alpha-receptor.** Life Sciences (Oxford). 16(9):1387-1392, 1975.

The involvement of the alpha-adrenergic receptor in the inhibition of cortisol induced tryptophan pyrrolase by norepinephrine was studied. Induction of hepatic tryptophan-2,3-dioxygenase in rats by cortisol or corticosterone was inhibited on treatment with norepinephrine. The beta-adrenergic blockers showed a small potentiating effect of the norepinephrine mediated inhibition. The alpha-adrenergic blockers significantly reversed this inhibition, suggesting that norepinephrine acts via the alpha-receptor in inhibition of the cortisol mediated induction of this enzyme. 14 references. (Author abstract)

221053 Medzihradsky, Fedor; Lin, Hsia-lien. Department of Pharmacology, University of Michigan Medical Center, Ann Arbor, MI 48104 **Inhibition of cellular ATP-hydrolyzing activity by tricyclic antidepressants and phenothiazine tranquilizers.** Life Sciences (Oxford). 16(9):1429-1440, 1975.

The inhibition of cellular adenosine triphosphate (ATP) hydrolyzing activity by tricyclic antidepressants (TA) and phenothiazine tranquillizers (PT) is reported. In leukocytes, preincubation of the cells with TA and PT resulted in up to 87% and 94% inhibition of the ATPase activity. Among TA, dibenzocycloheptadienes were somewhat more potent inhibitors than were derivatives of dibenzazepine. Substitution, at the position 2 of the phenothiazine nucleus, by a halogen and particularly by the CF3 group, increased the inhibitory strength of PT. Most effective in inhibiting ATPase was thioridazine, structurally differing from mesoridazine, the weakest inhibitor by a methylmercapto group instead of a methylsulfinyl substituent. The inhibition by the drugs was markedly reduced in the presence of millimolar ATP. The results indicate a possible adverse effect of these drugs on the cellular energy yielding capacity. 36 references. (Author abstract modified)

221131 Svensson, T. H.; Bunney, B. S.; Aghajanian, G. K. Department of Pharmacology, University of Goteborg, Fack S-400 33, Goteborg 33, Sweden **Inhibition of both noradrenergic and serotonergic neurons in brain by the alpha-adrenergic agonist clonidine.** Brain Research (Amsterdam). 92(2):291-306, 1975.

The inhibition of both noradrenergic and serotonergic neurons by clonidine is reported. By means of single unit recording techniques it was found that a small systemically administered (intravenous) dose of clonidine inhibited the spontaneous firing of brain norepinephrine (NE) containing neurons in the locus coeruleus. The NE neurons were consistently inhibited by the direct (microiontophoretic) application of minute amounts of NE or clonidine. Intravenous clonidine also inhibited firing of the great majority of 5-hydroxytryptamine (5-HT) neurons in the midbrain dorsal raphe nucleus. It is concluded that systemically administered clonidine inhibits the firing of brain NE neurons by acting directly upon adrenergic receptors located on or near the soma of these neurons but that the concomitant inhibition of 5-HT neurons is an indirect effect (possibly secondary to an impairment in noradrenergic transmission). 91 references. (Author abstract modified)

221188 Mundo, Antonio S.; Bonaccorsi, Aurora; Bareggi, Silvio R.; Franco, Rosetta; Morselli, Paolo L.; Garattini, Silvio. Department of Pharmacology, Faculty of Medicine, Granada, Spain **Relationships between tricyclic antidepressant concentrations, 1-3H-norafrenaline uptake and chronotropic effect in isolated rat atria.** European Journal of Pharmacology (Amsterdam). 28:368-375, 1974.

The uptake of imipramine-14C, desipramine-14C, amitriptyline-14C and chlorimipramine-14C was studied in rat isolated atria. Ths tissue levels were linearly related to the concentration in the incubation medium, the four lines sharing almost the same equation. Accumulation appeared to be a passive unsaturable process for each drug. Desmethyldoxepin, desmethylchlorimipramine, nortriptyline were four to five times less potent than desipramine in hibiting 1-3H-noradrenaline uptake, while the tertiary amines (imipramine, amitriptyline, chlorimipramine and doxepin) were far less potent. Apart from desipramine, which showed some sympathomimetic activity, the main effect of the drugs was a slowing of the spontaneous atrial rate which was more evident for the dimethyl than for the monomethyl compounds. All drugs potentiated 1-noradrenaline chronotropic response to varying degrees, but the potentiation of noradrenaline response was not always correlated with the inhibition of its uptake. Thus, inhibition of uptake is not a valid parameter for prediction of noradrenaline potentiation and vice versa. Drug tissue concentrations correlated with 1-3H-noradrenaline uptake inhibition but not with potentiation of 1-noradrenaline chronotropic response. 19 references. (Author abstract)

221267 Fanelli, Ottorino; Mazzoncini, V.; Trallori, L. Research Department, SIGMA-TAU S.p.A., I-00040 Pomezia (Rome) **Antagonism of psychostimulant 2-phenyl-5,5-dimethyl-tetrahydro-1,4-oxazine hydrochloride (G 130) to central nervous system depressing drugs: monoamine oxidase inhibitory activity and norepinephrine and serotonin induced changes, comparison with** Arzneimittel-Forschung (Aulendorf). 24(1):2025-2029, 1974.

Pharmacological interactions between 2-phenyl-5,5-dimethyl-tetrahydro-1,4-oxazine hydrochloride (G 130) and other central nervous system depressant drugs were studied in rats and mice, in comparison with dl-amphetamine. Furthermore, the monoamine oxidase (MAO) inhibiting activity and the changes induced in norepinephrine and serotonin levels in some tissues of rats were studied. The sleeping time induced by sodium pentobarbital is clearly antagonized by dl-amphetamine, whereas G 130 has practically no effect. On the contrary, G 130 and dl-amphetamine have the same effect in antagonizing the motor activity depressed by chlorpromazine. The reserine induced hypothermia and ptosis are also antagonized by both drugs. Also, norepinephrine and serotonin heart and brain levels are changed by both drugs but in a different way. Furthermore, anti-MAO activity of G 130 is much lower than that of dl-amphetamine. It is concluded that the psychostimulant action of G 130 with its previously demonstrated loss of tolerance, depends on a mechanism of action which is different from that of dl-amphetamine. 10 references. (Journal abstract modified)

221286 Mercier, J.; Dessaigne, S.; Menguy, A.; Manez, J. Laboratoire de Pharmacologie de la Faculte de Pharmacie, 27, Bd. J. Moulin, F-13 Marseille (5e), France **Electro-encephalographic study on the action of the combination meprobamate-acepromatezine on various cerebral systems.** Arzneimittel-Forschung (Aulendorf). 24(2):163-166, 1974.

The drug synergism observed in Mepronizine, a commercially available combination of meprobamate and acepromet azine, was examined through electroencephalographic studies of rabbits and cats. The combination exerts a synergistic depressant action on the reticular activating system of the rabbit and of the cat, explaining the hypnotic action of Mepronizine. In this association, meprobamate suppresses the slightly exciting effects exerted by acepromet azine on the cortical epileptogenic excitability, without deeply depressing the cortex. Further, the rhinencephalic excitability is only transiently and moderately depressed. 9 references. (Journal abstract modified)

221308 Kulkarni, S. K.; Dandiya, P. C. Department of Pharmacology, SMS Medical College, Jaipur-302004, India **Influence of chemical stimulation of central dopaminergic system on the open field behavior of rats.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 8(1):45-50, 1975.

The influence of substances known to selectively modify the brain levels of dopamine was studied on the open-field behavior of rats. Of the agents studied, l-dopa, benztropine and amantadine showed some similarity with amphetamine in inducing a high degree of complex stereotyped behavior in rats. The complex stereotyped behavior due to amphetamine and the similarity shown by these antiparkinsonian agents is explained based on brain dopamine levels. Apomorphine depressed the open-field behavior and produced a typical stereotyped biting in rats. Since 6-hydroxydopamine significantly prevented this biting behavior, it is suggested that the action of apomorphine is dependent on the presence of: 1) a particular functional state of catecholamine neurons; and 2) a separate receptor responsible for the behavioral actions of this drug. 36 references. (Journal abstract)

221640 Soderberg, Ulf. Neurofysiologiska laboratoriet, Ullerakers Sjukhus, 750 17 Uppsala, Sweden **/Hormone induced effects on lithium's pharmacokinetics./** Hormoniducerade effekter pa lithiums farmakokinetik. Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(6):473-475, 1974.

The effect of sex hormones and thyroid hormones on the pharmacokinetics of lithium was investigated in castrated and/or thyroidectomized rats of both sexes. Thyroxine conversion increased in all groups treated with lithium. Ovariectomized females suffered great thirst; thirst was reduced in males after castration. The affect of castration or ovariectomy on lithium induced thirst suggests that toxic effects of lithium may be hormone dependent. 6 references.

221647 Maitre, L.; Waldmeier, P. C.; Greengrass, P. M.; Jaekel, J.; Sedlacek, S.; Delini-Stula, A. Pharmaceuticals Division, CIBA-GEIGY, Basel, Switzerland **Maprotiline -- its position as an anti-depressant in the light of recent neuropharmacological and neurobiochemical findings.** Journal of International Medical Research (Northampton). 3(Suppl. 2):2-15, 1975.

Recent findings concerning the neuropharmacological and biochemical actions of maprotiline were reported at the Ludiomil Symposium, Stratford-upon-Avon, England, June 1974. The pharmacological results confirm previous data indicating that this a compound possesses antidepressant and psychosedative properties. In addition, both in rodents and primates, maprotiline reduces aggressive behavior. These effects occur in response to approximately the same doses as those necessary to induce specific antidepressant effects. Extensive biochemical investigations have shown that maprotiline treatment does not inhibit the uptake of serotonin into blood platelets from healthy volunteers. The binding of tryptophan to plasma proteins is also not affected. Maprotiline can thus be clearly distinguished from both imipramine and amitriptyline in its neuropharmacological and neurobiochemical activity spectrum. 24 references. (Author abstract modified)

221669 Daskalopoulos, N.; Schmitt, H.; Laubie, M. Faculte de Medecine, Paris-Broussais-Hotel-Dieu, 15, rue de l'Ecole-de-Medecine, 75006 Paris **/The action of delta9-tetrahydrocannabinol on central cardiovascular regulation: mechanism and localization./** Action du delta9-tetrahydrocannabinol sur la regulation cardiovasculaire centrale: mecanisme et localisation. Encephale (Paris). 1(2):121-132, 1975.

At the 9th International Congress of Neuropsychopharmacology, Paris, July 1974, a paper was presented in which the mechanism and localization of action of delta9-tetrahydrocannabinol (delta9-THC) on central cardiovascular regulation was investigated in cats and dogs. Delta9-THC induced a decrease in blood pressure and heartrate. This decrease appears to be centrally mediated. The splanchnic and cardiac discharges were reduced in intact animals as well as in debuffered cats, which rules out a reflex mediated action. The mechanism of this central decrease in sympathetic tone seems to be different from the reduction induced by clonidine or narcotic analgesic agents. The pressor response to high frequency stimulation of the medulla oblongata was abolished by small doses of delta9-THC. This agent did not reduce the pressor response to stimulation of the posterior hypothalamus induced by supramaximal stimulation and did not alter the hypertensive effect induced by stimulation of the cervical spinal cord. The medulla oblongata therefore appears to be the main site of action. 14 references. (Author abstract modified)

221736 Otsuka, M.; Tsuchiya, T.; Kitagawa, S. Sumitomo Chemical Co., Takarazuka Research Laboratories, 4-Takatsukasa, Takarazuka City, Hyogo, Japan **Electrophysiological and behavioral effects of 1-methyl-5-(o-fluorophenyl)-7-chloro-1,3-dihydro-2H-1,4-benz zodiazepin-2-one(ID-540) in cats and rabbits.** Arzneimittel-Forschung (Aulendorf). 25(5):755-760, 1975.

The effects of ID-540, 1-methyl-5-(o-fluorophenyl)-7-chloro-1,3-dihydro-2H-1,4-benzodiazepin- -one, on the central nervous system were evaluated electrophysiologically and behaviorally in cats and rabbits, using diazepam as a reference compound. ID-540 and diazepam produced muscle relaxation, grooming, facilitation of appetite and suppression of defensive behaviors. Though more effectively inducing an increase in fast activity and a decrease in frequency of hippocampal theta waves than diazepam, ID-540 scarcely affected the amplitude of subcortical electroencephalogram (EEG), which diazepam decreased in cats. ID-540 and diazepam increased the waking phase and decreased the paradoxical sleep phase. ID-540 and diazepam decreased the duration of amygdala afterdischarge in cats. ID-540 did not affect the duration of hippocampal afterdischarge whereas diazepam prolonged it. ID-540 more effectively depressed the hippocampal arousal response to stimulation of the ventromedial hypothalamus than did diazepam in rabbits. ID-540 depressed amygdalo - hippocampal evoked potential in cats, but did not affect norepinephrine induced pressor response. 16 references. (Journal abstract modified)

221737 Prepas, S.; Menon, M. K.; Clark, W. G. School of Medicine, University of California, Irvine, CA 92664 **Blockade of the central effects of d-amphetamine by amantadine II.** Arzneimittel-Forschung (Aulendorf). 25(5):780-782, 1975.

Research is reported which demonstrates that 1-adamantanamine (amantadine) pretreatment significantly reduces the motor hyperactivity and hyperthermia caused by d-

amphetamine in reserpinized mice. In drug naive mice, when amantadine was administered after d-amphetamine, the motor activity caused by the latter also was decreased. Since earlier studies show that amantadine pretreatment also antagonizes the increases in both motor activity and homovanillic acid in the caudate nucleus caused by d-amphetamine in mice, it is proposed that the mechanism is due to a competitive blockade at the presynaptic level in the brain. 12 references. (Journal abstract)

221740 Singh, K. P. Department of Pharmacology and Experimental Therapeutics, RNT Medical College, Udaipur, Rajasthan, India **Antiaccelerator and decelerator activity of eleven phenothiazine derivatives.** Arzneimittel-Forschung (Aulendorf). 25(4):526-529, 1975.

Eleven N-substituted phenothiazine derivatives were studied for their antiaccelarator and decelerator activities in the dog heart. The antiaccelarator activity was determined in dog heart - lung preparation. Taking into consideration the percentage inhibition of cardioacceleration produced by continuous infusion of 3 microgram/min of adrenaline, all drugs except chlorpromazine and 10-butyl-phenothiazine in two experiments caused more than 50% inhibition. 10-Propyl-phenothiazine induced maximum inhibitory effect. Two types of effects were observed upon impulse generation in the sinus node. Acceleration was produced by chlorpromazine, 10-cyclopentyl-phenothiazine, prothipendyl, and thiazinamium which was very short lived, whereas other drugs produced deceleration. The correlation between antiaccelerator and decelerator properties is a close one. 13 references. (Journal abstract)

221742 Jackson, D. M. Department of Pharmacology, University of Sydney, Sydney, N.S.W. 2006 **Beta-Phenylethylamine and locomotor activity in mice: interaction with catecholaminergic neurones and receptors.** Arzneimittel-Forschung (Aulendorf). 25(4):622-626, 1975.

The two phase effect of beta-phenylethylamine (PE) induced locomotor activity (LA) in mice was investigated. PE on injection into mice produces an early and late phase of increased LA. The early phase produced by 50mg PE/kg was inhibited by pretreatment with phenoxybenzamine, phentolamine, alpha-methyl-tyrosine, diethyldithiocarbamate, pimozide and haloperidol, but not by propranolol, protriptyline and reserpine. The late phase produced by 100mg PE/kg was blocked only by pimozide and haloperidol, both of these in doses at least ten times higher than those required to block the early phase. It is concluded that the increased early phase of LA is due to the release of dopamine by PE, but requires an intact dopamine and noradrenaline synthetic pathway, but not intact reserpine sensitive amine stores. In contrast, the late phase of LA is independent of catecholamine stores, produced by a direct action by either PE or metabolites on dopamine receptors. 25 references. (Journal abstract)

221743 Habiger, .Wilfried. Forschungsgruppe fur exper. Biologie, Teratologie und Onkologie, Nordwestdeutsche Kieferklinik, 2 Hamburg 20, Martinistr. 52 **/The effect of serotonin on the fetus and fetal-maternal relations in the rat./** Die Wirkung von Serotonin auf die Frucht und die feto-maternale Beziehung bei der Ratte. Arzneimittel-Forschung (Aulendorf). 25(4):626-632, 1975.

The effect of serotonin on the fetus in pregnant rats was examined. The lethality of serotonin is shown to increase with greater differentiation of the embryo. The results of serotonin injection in 15 day and 18 day pregnant rats was studied 6, 12, and 24h postadministration. Serotonin causes a contraction of the umbilical cord and hyperemia in the placenta. Further, a very quick necrotic process in the brain and liver of the fetus is evident. Simultaneous treatment of pregnant rats with serotonin and procarbazine or iproniazide, respectively, in small doses, intensifies the effect of serotonin. 36 references. (Journal abstract modified)

221859 Ishii, Yasuo; Homma, M.; Yoshikawa, A.; Umezawa, H. Nippon Kayaku Co., Pharmaceutical Division Research Laboratories, 3-31, Shimo, Kita-ku, Tokyo 115 **Pharmacological action of FD-008, a new dopamine-beta-hydroxylase inhibitor: III. Effects on endogenous biogenic amine levels in rats.** Arzneimittel-Forschung (Aulendorf). 25(3):383-385, 1975.

The effect of a new dopamine beta-hydroxylase inhibitor, 5-(4′-chlorobutyl)-picolinic acid (FD-008) on endogenous amine levels in various tissues of normotensive and spontaneously hypertensive rats were determined in comparison with its parent compound, fusaric acid, and disulfiram. FD-008 decreased norepinephrine (NE) levels in the brain and heart with a slight increase of dopamine (DA) level in the brain. NE lowering activity of FD-008 was stronger than that of fusaric acid. Disulfiram was less active, the activity 10% that of FD-008. FD-008 lowered NE level when DA was increased by pretreatment with L-dopa or iproniazid but did not cause a further significant reduction of NE when catecholamines were depleted by pretreatment with reserpine. 14 references. (Journal abstract)

221860 Benthe, H. F.; Gothert, M.; Krug, J. Pharmakologisches Institut der Universitat Hamburg, 2 Hamburg 20, Martinistr. 52, Germany **/Influence of reserpine on the potency of alpha-adrenoceptor blocking agents./** Beeinflussung der Wirkungsstarke von alpha-Rezeptorenblockern durch Reserpin. Arzneimittel-Forschung (Aulendorf). 25(3):402-407, 1975.

The influence of low doses of reserpine (0.125-2.0mg/kg) on the pressor effect of noradrenaline (NA) was studied in pithed rats, and the influence of reserpine pretreatment on the blocking activity of alpha-sympathicolytic agents was investigate.. Reserpine only increased the pressor effect of lower doses of NA without shifting the dose response curve to the left. The affinity of alpha-blocking agents to alpha-adrenoceptors is not altered in rats pretreated with reserpine. Only two phenylethylamine derivatives substituted with a p-hydroxy group possessed considerably higher blocking activity in reserpine pretreated animals than in rats not pretreated. The increase in sensitivity of blood vessels against low doses of NA observed in rats pretreated with reserpine is abolished even by alpha-blocking substances with low affinity to alpha-adrenoceptors. 8 references. (Journal abstract modified)

222639 Edmonds, Harvey Lee. University of California, Davis **A neuropharmacological evaluation of SC 13504 -- a new anticonvulsant. (Ph.D. dissertation).** Dissertation Abstracts International Ann Arbor, MI, Univ. M-films, No. 75-8326 HC$13.50 MF$5.00 298 p.

A neuropharmacological evaluation of SC 13504 was made to determine the character of its anticonvulsant and neurotoxic actions in several species. SC 13504 appears to possess a broad spectrum of anticonvulsant activity. It was effective against: 1) maximal electroshock seizures (MES) in rats; 2) pentylenetetrazol seizures (PTZ) in rats; 3) electrically induced cortical afterdischarges (EICA) in rats and cats; 4) electrically induced hippocampal afterdischarges (EIHA) in rats, cats and dogs; and 5) penicillin induced cortical afterdischarges (PICA) in rats and cats. These results suggest that the magnitude of

anticonvulsant and neurotoxic effects of SC 13504 is species related. The compound seems to be most potent and least toxic in the rat. A reasonable explanation for this lack of toxicity is the biotransformation of SC 13504 to an active but nontoxic metabolite. SC 13504 has its lowest margin of safety in the cat, but both the cat and dog appear to rapidly develop tolerance to its overt neurotoxic effects. (Journal abstract modified)

222640 Dubas, Thea Christa. University of Western Ontario, Canada **Effects of analgetics on centrally-induced "pain" in rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ottawa, National Library of Canada

The technique of intracranial aversive stimulation was employed in rats to determine whether brain areas which play different functional roles in central pain mechanisms have a different pharmacological sensitivity to analgesic agents. Dose response curves for the depressant effects of five narcotic analgetics, morphine, heroin, fentanyl, propoxyphene, tilidine and of the phenothiazine derivative, levomepromazine, on the escape response elicited by suprathreshold stimulation of these areas were obtained. When the effects of each drug in the various brain areas were compared, it was found that each narcotic analgetic was associated with a family of parallel dose response curves whereas levomepromazine produced two sets of parallel dose response curves. There was some commonality of action among all of the analgetics investigated. On the basis of the differential sensitivity exhibited by the various brain areas, it was concluded that analgesia of the morphine type involves: first an alteration in the integrating activities of the nonspecific, associational and specific sensory thalamic nuclei; second, an influence upon the structures of the limbic system; third, and action upon the perceptual and behavioral responses mediated by the dorsal midbrain; and, fourth, an impairment of sensory impulse transmission within the main somesthetic conduction pathway. (Journal abstract modified)

222641 Shih, Tsung-Ming. University of Pittsburgh **Effects of methylphenidate hydrochloride on the central nervous system. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-13216 HC$13.50 MF$5.00 155 p.

The effects of methylphenidate HCl on selective sensory information processes were investigated in rats. In rats, pretreatment with tetrabenazine or haloperidol completely prevented the inhibitory effect of methylphenidate on the mesencephalic reticular formation (MRF) spontaneous multiple unit activity (MUA), suggesting that the central effects of methylphenidate are mediated through catecholamines, especially dopamine. Further studies showed that oxotremorine in rats and cats and nicotine in rats mimicked the effects of methylphenidate. Mecamylamine HCl completely blocked the effect of nicotine and methylphenidate, whereas atropine sulfate counteracted completely the effect of oxotremorine and only slightly that of methylphenidate, indicating a possible nicotinic site of action of methylphenidate. These findings suggest that methylphenidate might exert a quieting effect on the overactivated MRF in hyperkinetic children. The drug's effect also suggests a possible causative relationship between the hyperarousal state and a deficit or immaturity of the inhibitory role of the MRF. (Journal abstract modified)

222644 Bigler, Erin David. Brigham Young University **Modulation of photically evoked after-discharges by means of pharmacological and behavioral arousal. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-11974 HC$13.50 MF$5.00 111 p.

The modulation of photically evoked afterdischarges by means of pharmacological and behavioral arousal was reported in rats. Pharmacological arousal induced by systematic applications of pilocarpine, physostigmine, or amphetamine, as contrasted with control substances of atropine, methyl atropine, or saline, markedly attenuated photically evoked afterdischarge (PhAD) parameters in restrained and nonrestrained albino rats. Pilocarpine, physostigmine, or amphetamine treatments reliably induced sustained bouts of dorsal hippocampal theta activity as well as changes in locomotor activity. Atropine, only at high doses, altered PhAD parameters and locomotor activity. Using incremental dosages, dose response effectiveness was determined for each drug. In separate experiments, behavioral arousal was also manipulated. Increased behavioral arousal induced by contingent tail shocks or decreased behavioral arousal following habituation to the photic stimulus attenuated PhAD parameters. (Journal abstract modified)

222803 Tothill, Anne. Department of Pharmacology and Therapeutics, Middlesex Hospital Medical School, Cleveland St., London W1 **The effect of autonomic and psychotropic drugs on adrenaline reversal in the rat uterus.** European Journal of Pharmacology (Amsterdam). 32(2):221-226, 1975.

Desipramine and other psychotropic and autonomic drugs were tested for their ability to prevent the motor response of the rat uterus to adrenaline in vitro. Those agents which have been shown to prevent catecholamine uptake into stores most readily reversed the motor response; those which had little or no effect on catecholamine storage were usually without effect on the motor response to adrenaline. The motor response of the rat uterus to adrenaline is due to prostaglandin E2. Agents blocking the motor response prevented the release of prostaglandin and did not block action of prostaglandin on the uterus. Since all the effective agents also interfered with uptake with catecholamine stores it is hypothesized that passage of catecholamine in and out of storage depots is involved with the synthesis of prostaglandins. 8 references. (Author abstract)

222804 Clineschmidt, Bradley V.; Pflueger, A. Barbara; Bunting, Patricia R.; McGuffin, Jodie C.; Ballentine, Ruby J. Merck Institute for Therapeutic Research, West Point, PA 19486 **Central catecholamine receptor blocking actions of BE-2254 ('HEAT'): comparison with chlorpromazine and haloperidol.** European Journal of Pharmacology (Amsterdam). 32(2):279-286, 1975.

Central catecholamine receptor blocking actions of BE-2254 ('HEAT') were compared with chlorpromazine and haloperidol in the rat. BE-2254, 2-(beta-(4-hydroxyphenyl)-ethylaminomethyl)-tetralone, was about equal to chlorpromazine as an antagonist of central noradrenergic receptor stimulation produced by clonidine (enhancement of the flexor or reflex in spinalized rats). Haloperidol and phentolamine had essentially no effect at 9mg/kg i.p. At higher doses, BE-2254 also blocked central receptors for dopamine. BE-2254 antagonized amphetamine stimulated locomotor activity in mice, providing additional evidence that the compound can significantly inhibit central catecholamine receptor mediated responses. It is concluded that BE-2254 blocks receptors for both norepinephrine and dopamine in the central nervous system -- the former at lower doses than the latter. It appears that this agent is useful for producing blockade of central receptors for norepinephrine. 17 references. (Author abstract modified)

222805 Nyback, Henrik V.; Walters, Judith R.; Aghajanian, George K.; Roth, Robert H. Department of Pharmacology,

Karolinska Institute, S-104 01 Stockholm **Tricyclic antidepressants: effects on the firing rate of brain noradrenergic neurons.** European Journal of Pharmacology (Amsterdam). 32(2):302-312, 1975.

The spontaneous activity of the norepinephrine containing cells of the locus coeruleus was recorded in chloral hydrate anesthetized rats. The effect of seven tricyclic antidepressants on the firing rate of single cells in the locus coeruleus was studied. All the drugs tested, except iprindole, markedly decreased the rate of firing of the noradrenergic cells. Antidepressants having a secondary amine in the side chain, desipramine, nortriptyline and chlordesipramine, were more potent than their respective tertiary amine analogs, imipramine, amitriptyline and chlorimipramine. The results show that secondary amine antidepressants are more potent than their tertiary amine homologs in blocking the uptake of norepinephrine into brain and peripheral tissues. Despite their lower potency it is concluded that tertiary antidepressants act on noradrenergic neurons in their unchanged form and not via secondary amine metabolites formed during the recording experiments, since alternations in liver metabolism did not influence the response. 61 references. (Author abstract modified)

222813 Harris, Jane E.; Baldessarini, R. J.; Roth, R. H. Department of Pharmacology, Emory University Medical School, Atlanta, GA 30322 **Amphetamine-induced inhibition of tyrosine hydroxylation in homogenates of rat corpus striatum.** Neuropharmacology (Oxford). 14(7):457-471, 1975.

Tyrosine hydroxylase activity was measured in vitro in the rat brain by following the rate of production of 14CO2 from (14C)-dopa newly formed from L-(1-14C)-tyrosine in a crude synaptosomal preparation of striatal homogenates which contained only endogenous pteridine cofactor. Administration of (+)-amphetamine in vivo led to a specific local inhibition of tyrosine hydroxylase activity. When striatal nerve endings were exposed directly to amphetamine in vitro, stimulation rather than inhibition of tyrosine hydroxylation occurred, although the hydroxylated metabolites p-hydroxyamphetamine and p-hydroxynorephedrine inhibited the reaction. Inhibitory effects of in vivo administration of amphetamine on tyrosine hydroxylase activity in striatal synaptosomes may similarly be mediated by a decreased impulse flow in striatal dopamine neurons. The inhibitory effect of (+)-amphetamine was interrupted by blockade of striatal dopamine receptors with chlorpromazine and by blockers of gamma-aminobutyric acid receptors. Local striatal receptors of dopamine may thus be involved in this action of amphetamine or descending gamma-aminobutyric acid neurons may mediate a neurophysiological feedback regulation of activity in the nigrostriatal pathway. 53 references. (Author abstract modified)

222819 Boyd, Eleanor H.; Boyd, E. S.; Brown, L. E. Department of Pharmacology and Toxicology, University of Rochester School of Medicine and Dentistry, Rochester, NY 14642 **Differential effects of a tetrahydrocannabinol and pentobarbital on cerebral cortical neurones.** Neuropharmacology (Oxford). 14(7):533-536, 1975.

The effects of a tetrahydrocannabinol and pentobarbital on cerebral cortical slices were examined in the monkey. Stimulation of somatosensory cortex in the unanesthetized pontine or encephale isole squirrel monkey evoked early and late surface responses and corresponding unit firing, sometimes followed by later repetitive surface waves and unit bursts in ipsilateral and contralateral postarcuate cortex. Pentobarbital abolished the late surface responses, the corresponding late unit firing, the later surface waves, and the corresponding unit bursts, whereas delta9-tetrahydrocannabinol had opposite effects. It augmented the late surface responses, the late unit firing, and the later surface waves, and it accentuated the later unit bursts. 8 references. (Author abstract)

222821 Hadfield, M. Gary; Weber, Nicholas E. Box 17, MCV Station, Richmond, VA 23298 **Effect of fighting and diphenylhydantoin on the uptake of 3H-1-norepinephrine in vitro in synaptosomes isolated from retired male breeding mice.** Biochemical Pharmacology (Oxford). 24(16):1538-1540, 1975.

The effect of fighting and diphenylhydantoin (DPH) on the uptake of 3H-1-norepinephrine (NE) was examined in vitro in synaptosomes isolated from retired male breeding mice. The uptake of 3H-NE was significantly altered by fighting and by DPH in synaptosomes isolated from white Swiss male mice retired from breeding activity. These results demonstrate an adaptive change in the membrane affinity for NE after an acute stress situation. The adaptation is apparently at two loci. First, the increased Michaelis constant for NE in fighting as compared with nonfighting animals reflects a decreased affinity of the NE carrier for its substrate. The second change, increased maximum velocity may indicate an increased number of NE carriers or greater utilization of existing carriers. The increase in uptake of NE in nerve terminals produced by fighting has been shown to be significantly decreased by DPH. This inhibition of NE uptake may represent the mechanism by which, in the studies previously cited, DPH abolished fighting in animals. 19 references.

222822 Cho, Arthur K.; Schaeffer, James C.; Fischer, Joseph F. Department of Medicine, UCLA School of Medicine, Center for the Health Sciences, Los Angeles, CA 90024 **Accumulation of 4-hydroxyamphetamine by rat striatal homogenates.** Biochemical Pharmacology (Oxford). 24(16):1540-1541, 1975.

The behavior of p-hydroxyamphetamine-3H (p-OHA-3H) in rat striatal preparations that accumulate dopamine-3H (DA-3H) was examined. The uptake of DA was three times that of p-OHA and 150 times that of amphetamine. The accumulation of DA and p-OHA was sensitive to osmotic shock. With DA as the substrate; p-OHA and amphetamine were equipotent as inhibitors; DA was a potent inhibitor of p-OHA uptake. Amphetamine was more effective as an inhibitor of DA uptake than of p-OHA uptake. The results suggest that p-OHA is accumulated by a process that is temperature dependent as well as sodium dependent and is similar to DA uptake in its sensitivity to a variety of different inhibitors. In contrast, amphetamine was not appreciably accumulated by this system. 20 references.

222889 Popova, N.; Kritvitskaya, G. N. Institut mozga AMN SSSR, Moscow **/The influence of several psychotropic drugs on the structure of the brain./** Vliyaniye nekotorykh psikhotropnykh sredstv na struktury mozga. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 75(7):1064-1069, 1975.

The influence of LSD and indopan on cerebral structure was investigated in white rats. Histological analysis was performed several hours after drug injection. Both indopan and LSD were found to induce similar structural changes in the neuron and interneuronal relations; differences in localization of the changes was noted in the functionally different brain systems. Both the sensormotor cortex and the subcortical formations of the brain rich in dopamine and serotonin manifested high sensitivity to indopan. The central effects of LSD were determined by the drug's influence on both the synapses and the cell body components of different brain systems, particularly

the visual system. The morphological changes induced by both drugs were concluded to be functional in nature. 25 references. (Journal abstract modified)

222890 Matvyeyev, V. F.; Vorob'yev, V. S. Moskovskogo meditsinskogo stomatologicheskogo instituta, Moscow **/Some peculiarities of the neuron ultrastructure in the brain cortex motor area under the influence of lysergic acid diethylamide (LSD) and haloperidol./** Nekotoryye osobennosti ul'trastruktury neyronov dvigatel'noy oblasti kory golovnogo mozga pri vozdeystvii lizergamida (LSD) i galoperidola. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 75(7):1070-1076, 1975.

The effect of haloperidol and combined LSD/haloperidol administration on the ultrastructure of motor cortex neurons was investigated in rats. Histological analysis was carried out with an electron microscope at 1, 4, 8, 12, and 24 hour intervals following drug administration. LSD caused neuron swelling, and haloperidol caused an increase in the number of large neurons with a hyperchronic cytoplasm staining and increased intensively stained nuclei. Haloperidol also elicited a significant increase in the surface of the rough endoplendoplasmic reticulum and ribosomes observed in the large hyperchronic neurons. Haloperidol was concluded to have a protective influence on the development of LSD intoxication. 21 references. (Journal abstract modified)

223012 Roshchina, L. F.; Al'Tshuler, R. A.; Mashkovskiy, M. D. Laboratoriya farmakologii, Vsesoyuznogo nauchno-issledovatel'skogo khimiko-farmatsevticheskogo instituta, Moscow **/Comparative effects of sydnocarb and amphetamine on the bioelectrical activity of the brain./** Sravnitel'noye vliyaniye sidnokarba i fenamina na bioelektricheskuyu aktivnost' golovnogo mozga. Farmakologiya i Toksikologiya (Moskva). 38(3):263-267, 1975.

The effects of intraperitoneal injection of sydnocarb and amphetamine on cerebral bioelectrical activity was investigated in cats and rabbits. Sydnocarb was found to produce a more lasting reticular - cortical activation than amphetamine. Electroencephalograms also indicated a substantial difference in the nature of interaction of sydnocarb and amphetamine with chlorpromazine, reserpine and imipramine. The activating effect of sydnocarb was diminished by the introduction of reserpine, imipramine and chlorpromazine; while the activating effect of amphetamine was enhanced by their introduction. 29 references. (Journal abstract modified)

223014 Arushanyan, Ye. B.; Tolpyshev, B. A. Chitinskogo meditsinskogo instituta, Chita, U.S.S.R. **/The dopaminergic component in the action of d,1-amphetamine on the inhibitory function of the caudate nucleus./** O dafaminergicheskom komponente v deystvii fenamina na tormoznuyu funktsiyu khvostatogo yadra. Farmakologiya i Toksikologiya (Moskva). 38(3):269-272, 1975.

The effect of various catecholamines on d,1-amphetamine influence on the inhibitory function of the caudate nucleus was investigated in cats. Cats were subjected to low frequency stimulation of the head of the caudate nucleus. Arrest reactions and caudate spindles were registered in the sensorimotor cortex, contralateral caudate nucleus and mesencephalic reticular formation. Under normal conditions, amphetamine was found to raise the threshold of behavioral and electroencephalogram indices of caudate inhibition. Preliminary injection of alpha-methyltyrosine was found to blunt the action of amphetamine; disulfiram administration had no effect on amphetamine activity. 14 references. (Journal abstract modified)

223016 Absava, G. I.; Artemenko, G. N.; fon Littrov, K.; Vikhlyayev, Yu. I. Laboratoriya psikhofarmakologii, Instituta farmakologii AMN SSSR, Moscow **/The correlation between triftazine distribution in some rat organs and its pharmacological effects with different types of administration./** O sootnoshenii mezhdu raspredeleniyem triftazina v nekotorykh organakh krys i yego farmakologicheskimi effektami pri raznykh sposobakh vvedeniya. Farmakologiya i Toksikologiya (Moskva). 38(3):277-281, 1975.

The correlation between the dynamics of triftazine distribution in the brain, liver and blood plasma and the dynamics of the drugs cataleptic, antiaggressive and motor coordination effects were investigated in rats. Following oral triftazine administration, the drug was slowly absorbed in the liver; intramuscular administration led to faster and more even drug distribution. The pharmacological effects of triftazine occur more rapidly following intramuscular administration because of the speed with which the neuroleptic reaches the brain. 20 references. (Journal abstract modified)

223017 Arefolov, V. A.; Panasyuk, L. V.; Firsov, V. K. Laboratoriya farmakologii nervnoy sistemy, Instituta farmakologii AMN SSSR, Moscow **Neurotransmitter content in synaptic vesicles of the adrenergic nerves of rats under pharmacological influence./** Soderzhaniye neyromediatora v sinapticheskikh puzyr'kakh adrenergicheskikh nervov krysy pri nekotorykh farmakologicheskikh vozdeystviyakh. Farmakologiya i Toksikologiya (Moskva). 38(3):285-298, 1975.

The content of neurotransmitters in the synaptic vesicles of the adrenergic nerve fibers of the vas deferens was investigated in rats following depletion of the mediator's reserves by tyramine and the subsequent exogenous norepinephrine accumulation. Cytochemical electron microscopy was used to measure the effect of antidepressants on the accumulation of exogenous norepinephrine in the synaptic vesicles. The antidepressants blocked norepinephrine accumulation when the mediator was introduced in concentrations of 0.5micrograms/ml. Norepinephrine accumulation was not impeded, however, when the mediator's concentration was increased to .03 mg/ml. 9 references. (Journal abstract modified)

223018 Chichkanov, G. G. Laboratoriya farmakologii serdechno-sosudistoy sistemy Instituta farmakologii AMN SSSR, Moscow **/The effect of tranquilizers (diazepam and chlordiazepoxide) on the blood supply and cardiac activity./** Vliyaniye trankvilizatorov (diazepama i khlordiazepoksida) na krovosnabzheniye i deyatel'nost' serdtsa. Farmakologiya i Toksikologiya (Moskva). 38(3):303-307, 1975.

The effects of diazepam and chlordiazepoxide on blood supply and cardiac activity were investigated in cats anesthetized with urethane and chloralose. Both compounds were found to lower vascular resistance to blood flow, thereby lowering coronary circulation rate and oxygen intake by the heart. Diazepam elicited appreciable hypertension and bradycardia and reduced cardiac output. Chlordiazepoxide produced a smaller decline in arterial pressure and bradycardia and reduced cardiac output. Unlike chlordiazepoxide, diazepam reduced myocardium contractility as manifested by decreased maximum blood flow acceleration in the aorta and an increase in systolic contraction time. The more pronounced hypertension elicited by diazepam was attributed to inhibition of myocardium contractility. 25 references. (Journal abstract modified)

223049 Hirano, Makoto; Uchimura, Hideyuki; Saito, Masashi. Laboratory of Neurochemistry, Hizen National Mental

Hospital, Kanzaki, Saga 842-01, Japan **Regional distribution of monoamine oxidase activity for 5-hydroxytryptamine and tyramine in the hypothalamus of the rat.** Brain Research (Amsterdam). 93(3):558-563, 1975.

The regional distribution of monoamine oxidase (MAO) in the hypothalamus of the rat was examined using 5-hydroxytryptamine (5-HT) and tyramine as substrates. MAO activities toward 5-HT and toward tyramine were detected in all nuclei and were found to be unevenly distributed in the hypothalamus. The highest 5-HT - MAO activities were found in the nuclei of the ventromedialis, premammilaris ventralis, paraventricularis, and dorsomedialis. Extremely high concentrations of tyramine - MAO were found in the nucleus paraventricularis and the nuclei of medial and posterior parts of arcatus. In several hypothalamic nuclei, the distribution of 5-HT - MAO was different from that of 5-HT levels. The results suggest that multiple forms of MAO exist in individual hypothalamic nuclei and also that the relative distribution of 5-HT - MAO and tyramine - MAO is different in the hypothalamus. 26 references.

223050 Versteeg, D. H. G.; Wurtman, R. J. Department of Nutrition and Food Science, MIT, Cambridge, MA 02139 **Effect of ACTH4-10 on the rate of synthesis of (3H)catecholamines in the brains of intact, hypophysectomized and adrenalectomized rats.** Brain Research (Amsterdam). 93(3):552-557, 1975.

The effect of adrenocorticotropic hormone (ACTH4-10) on the rate of synthesis of (3H)catecholamines was examined in the brains of intact, hypophysectomized and adrenalectomized rats. The rate of synthesis of (3H)catecholamines in the brains of intact rats was significantly increased following administration of ACTH4-10. Neither in adrenalectomized rats nor in corticosterone treated adrenalectomized rats could an effect be observed of ACTH4-10 on the accumulation of brain (3H)norepinephrine and (3H)dopamine or (3H)catecholamines. The findings suggest that the effect of ACTH4-10 on catecholamine metabolism in the brain is indirect, that is, it is mediated by a pituitary or adrenal factor. 16 references.

223051 Siegel, Laurane G.; McClure, William O. Department of Biochemistry, University of Illinois, Urbana, IL 61801 **Putrescine: effect on axoplasmic transport.** Brain Research (Amsterdam). 93(3):543-547, 1975.

The movement of putrescine along the optic nerve tract fibers of the rat was examined in a study of axoplasmic transport. In the optic tract, a large difference between the levels of radioactivity arising from 1-(3H)proline and from (3H)putrescine suggested that no transport of putrescine occurred. Low doses of putrescine were found to depress radioactive transport by a small amount while complete inhibition of transport was found with doses of putrescine over 300 micrograms. It is concluded that the drug affects neither the uptake of amino acids into the cell nor their subsequent incorporation into proteins since the synthsis of proteins in the retina was not depressed by putrescine. The results suggest that putrescine is involved in the cellular control of axoplasmic transport and as such may involve an element of cooperativity. 14 references.

223053 Suzuki, Osamu; Nagase, Fumihiko; Yagi, Kunio. Institute of Biochemistry, Faculty of Medicine, University of Nagoya, Nagoya, Japan **Tryptophan metabolism in developing chick brain.** Brain Research (Amsterdam). 93(3):455-462, 1975.

The normal patterns of the occurrence of tryptophan, 5-hydroxytryptamine (5-HT), 5-hydroxyindoleacetic acid (5-HIAA) and monoamine oxidase (MAO) activity in chick brain during development were investigated. Tryptophan level in the brain on the seventh day of embryonic development was rather high and decreased gradually until day 17, but increased markedly from day 17 to hatching, then increased slightly from hatching to day 14 after hatching. 5-HT, 5-HIAA and MAO were already present on the seventh day of incubation, increased gradually with a temporary peak on day 14, and increased remarkably from day 17 to hatching, after which they reached a plateau and remained unchanged from days 7 to 14 after hatching. Since the increase between day 17 and hatching was observed in the patterns of tryptophan, 5-HT, 5-HIAA and MAO activity, the critical period of tryptophan metabolism in the brain during development seems to exist in this period. 5-HT was increased markedly, even in newborn chick brain. This might indicate that the activity of tryptophan hydroxylase in newborn chick brain would be as high as that in adult chick brain. 21 references. (Author abstract modified)

223054 Roberts, D. C. S.; Zis, A. P.; Fibiger, H. C. Division of Neurological Sciences, Department of Psychiatry, University of British Columbia, Vancouver, British Columbia **Ascending catecholamine pathways and amphetamine-induced locomotor activity: importance of dopamine and apparent non-involvement of norepinephrine.** Brain Research (Amsterdam). 93(3):441-454, 1975.

In a study of the ascending catecholamine pathways and amphetamine induced locomotor activity, stereotaxically placed intracerebral microinjections of 6-hydroxydopamine (6-OHDA) were used to produce selective and extensive lesions of either the dopaminergic nigro - neostriatal bundle or the dorsal and ventral noradrenergic projections in the rat. The extensive damage of the noradrenergic pathways which is typically obtained after intranigral 6-OHDA injections was completely prevented by pretreatment with desipramine. Extensive depletions of norepinephrine (NE) in the hypothalamus, cerebral cortices and hippocampi failed to influence either spontaneous or d-amphetamine induced locomotor activity. Selective depletion of neostriatal dopamine (DA) after intranigral 6-OHDA injections severely reduced but did not abolish amphetamine induced hyperkinesia. These data are consistent with the view that ascending DA projections are a critical substrate for amphetamine induced hyperkinesia. They furthermore suggest that ascending NE systems do not play a role in this response. 36 references. (Author abstract modified)

223063 Mayzelis, M. Ya. Moskovskii nauchno-issledovatel'skii institut psikhiatrii, Ministerstva zdravookhraneniya RSFSR, Moscow **/The effect of the psychotropic agents (chlorpromazine, majeptil, tricedil) on protein synthesis in various portions of the rat brain./** O vliyanii psikhotropnykh sredstv (aminazin, mazheptil, trisedil) na sintez belka v raznykh otdelakh mozga krys. Byulleten' eksperimental'noy biologii i meditsiny (Moskva). 79(5):62-64, 1975.

The effects of chlorpromazine, majeptil and tricedil were investigated on methionine-S35 incorporation into the total proteins in various sections of the rat brain. Generalized depression of protein synthesis was manifested in all structures except the medulla oblongata 1-3 hours following chlorpromazine administration. Majeptil was found to have a stimulating effect on most sections of the brain. Tricedil catalyzed a reduction of methionine-S35 incorporation into the proteins of most brain structures and an increase in its incorporation into the olfactory lobes. Changes in the protein synthesis in individual structures of the brain were concluded to provide an important link in the action mechanism of psychotropic

preparations on the organism. 20 references. (Journal abstract modified)

223171 Segal, Menahem. Isotope Department, Weizmann Institute of Science, Rehovot, Israel **Physiological and pharmacological evidence for a serotonergic projection to the hippocampus.** Brain Research (Amsterdam). 94(1):115-131, 1975.

Rat hippocampal pyramidal cells were studied for their response to serotonin (5-HT) applied iontophoretically and to stimulation of the midbrain raphe nuclei. Ninety two percent of the cells studied were inhibited by 5-HT. Forty eight percent of the cells responded by inhibition to dorsal and median raphe stimulation. The inhibitory response to raphe stimulation was absent when the rats were pretreated with p-chlorophenylalanine (PCPA), a 5-HT synthesis inhibitor; PCPA effects were alleviated by 5-hydroxytryptophan or 5-HT administration. The response to raphe stimulation was blocked by methysergide and cyproheptadine. The responses to raphe stimulation were potentiated by chlorimipramine, a 5-HT reuptake blocker. These data satisfy several of the criteria required to identify 5-HT as the inhibitory neurotransmitter for the raphe - hippocampal pathway. 46 references. (Author abstract)

223174 Da Prada, M.; Saner, A.; Burkard, W. P.; Bartholini, G.; Pletscher, A. Research Division, F. Hoffmann-La Roche, Basel, Switzerland **Lysergic acid diethylamide: evidence for stimulation of cerebral dopamine receptors.** Brain Research (Amsterdam). 94(1):67-73, 1975.

Evidence that lysergic acid diethylamide (LSD) decreases the dopamine (DA) turnover in the central nervous system of rats as a consequence of DA receptor stimulation is presented. In the rat, LSD decreased the straital and retinal content of homovanillic acid. LSD did not change the level of DA, but delayed the alpha-methyl-p-tyrosine induced disappearance of this amine in the forebrain. In the cat, LSD diminished the DA output into the perfusate of the caudate nucleus. Furthermore, LSD increased the activity of adenylate cyclase in straital homogenates of rat. These and other findings indicate that in the central nervous system LSD stimulates DA receptors which may be involved in LSD induced psychosis. 38 references. (Author abstract)

223175 Von Hungen, Kern; Roberts, Sidney; Hill, Dane F. Department of Biological Chemistry, School of Medicine, University of California, Los Angeles, CA 90024 **Interactions between lysergic acid diethylamide and dopamine sensitive adenylate cyclase systems in rat brain.** Brain Research (Amsterdam). 94(1):57-66, 1975.

The interactions of the hallucinogenic drug, D-lysergic acid diethylamide (D-LSD), and other serotonin (5-HT) antagonists with catecholamine sensitive adenylate cyclase systems in cell free preparations from different regions of rat brain were examined. In equimolar concentration, D-LSD, 2-bromo-D-lysergic acid diethylamide (BOL), or methysergide strongly blocked maximal stimulation of adenylate cyclase activity by either norepinephrine (NE) or dopamine (DA) in particulate preparations from cerebral cortices of young adult rats. D-LSD also eliminated the stimulation of adenylate cyclase activity by equimolar concentrations NE or DA in particulate preparations from rat hippocampus. The stimulatory effects of D-LSD and DA were also inhibited by the 5-HT blocking agents, BOL, 1-methyl-D-lysergic acide diethylamide , and cyproheptadine, but not by the beta-adrenergic blocking agent, propranolol. However, these 5-HT antagonists by themselves were incapable of stimulating adenylate cyclase activity in the straital preparations. 28 references. (Authro abstract modified)

223562 Holcslaw, Terry Lee. Purdue University **A study of the relationship between circadian rhythms in drug action and metabolism in the mouse. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-10892 HC$13.50 MF$5.00 151 p.

The observation of Radzialowski and Bousquet (1968) of a circadian rhythm in the in vitro oxidative metabolism of hexobarbital, p-nitroanisole, and aminopyrine by the mouse was extended to demonstrate a circadian variation in the in vivo metabolism of meperidine, as well as daily variations in the response of mice to meperidine and hexobarbital. The nature of the association between circadian variations in responsiveness of mice to metabolism of meperidine and hexobarbital was the major focus. Results support the contention that the circadian rhythmic variation in meperidine and hexobarbital metabolism could subserve the circadian rhythmic variation in response of mice to these drugs. Furthermore, data indicate that time dependent changes in central nervous system sensitivity to hexobarbital may also be related to the daily rhythm in duration of hexobarbital induced hypnosis. (Journal abstract modified)

224096 Zatz, Martin; Kebabian, John W.; Romero, Jorge A.; Lefkowitz, Robter J.; Axelrod, Julius. Section on Pharmacology, Laboratory of Clinical Science, Bldg. 10, Room 2D47, NIMH, Bethesda, MD 20014 **Pineal beta-adrenergic receptor: correlation of binding of 3H-(1)-alprenolol with stimulation of adenylate cyclase. (Unpublished paper).** Bethesda, MD, NIMH, 1975. 32 p.

Studies of the binding of 3H-(1)-alprenolol, a potent competitive beta-adrenergic antagonist, to sites in membranes of the rat pineal gland are reported. The properties of these binding sites were compared to those of the receptors which mediate the beta-adrenergic activation of pineal adenylate cyclase. Both sites are highly stereospecific. The (1)-stereoisomers of alprenolol and propranolol were at least two orders of magnitude more potent than the (d)-stereoisomers in inhibiting isoproterenol stimulated adenylate cyclase activity of 3H-(1)-alprenolol binding. The dissociation constants of the (1)-stereoisomers of both alprenolol and propranolol were determined by competition for binding sites or by inhibition of isoproterenol stimulated adenylate cyclase. Beta-adrenergic agonists which stimulated adenylate cyclase also competitively inhibited the binding of 3H-(1)-alprenolol. They showed the same order of potency and the same individual affinities in the two systems. Alpha-adrenergic blockers were ineffective in inhibiting either adenylate cyclase stimulation or 3H-(1)-alprenolol binding. Isoproterenol stimulation of adenylate cyclase activity and 3H-(1)-alprenolol binding were rapid and rapidly reversible. Findings suggest that the binding of 3H-(1)-alprenolol occurs at sites indistinguishable from the pineal beta-adrenergic receptor. 33 references. (Author abstract modified)

224114 Rayevskiy, K. S.; Maysov, N. I. Laboratoriya farmakologii nervnoy sistemy, Instituta farmakologii AMN SSSR, Moscow **/The effect of neuroleptics and antidepressants on the uptake of 3H-gamma-aminobutyric acid by isolated nerve endings of the rat brain./** Vliyaniye nyroleptikov i antidepressantov na protsess zakhvata gamma-aminomaslyanoy kislotyH3 izolirovannymi nervnymi okonchaniyami mozga krysy. Byulleten' Eksperimental'noy bilogii i meditsiny (Moskva). 79(6):63-65, 1975.

The effect of neuroleptics and antidepressants was investigated on 3H-gamma-aminobutyric acid (GABA-H3) accumulation in the synaptosomes of the rat cerebral cortex.

Phenothiazine neuroleptics tested included chlorpromazine, trifluoperzine and fluphenazine. Antidepressants used included imipramine and thorazicine. All neuroleptics were found to inhibit the process of neurotransmitter uptake by the cerebral synaptosomes. Antidepressants were found to be less potent. Chlorpromazine had the greatest inhibitory effect on GABA uptake, and thorazicine had the smallest effect. The influence of neuroleptics on GABA uptake was tentatively concluded to affect the mode of a synaptic action of these drugs. 14 references. (Journal abstract modified)

224115 Arefolov, V. A.; Panasyuk, L. V. Laboratoriya farmakologii nervnoy sistemy, instituta farmakologii AMN SSSR, Moscow /**The effect of carbidine on adrenergic transmission.**/ Vliyaniye karbidina na protsess adrenergicheskoy neyroperedachi. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 79(6):66-69, 1975.

The effect of an original psychotropic agent, carbidine, on the process of adrenergic neurotransmission was investigated in an isolated vas deferens of a rat. Noradrenaline content in the vas deferens was determined spectrofluorimetrically. The capacity of the neuroleptic to block vas deferens consumption of the exogenous noradrenaline was also measured. Carbidine was found to possess an andrenomimetic effect due to release noradrenaline, thus leading to a reduction of endogenous neuromediator reserves. 6 references. (Journal abstract modified)

225059 Tehrani, Jamshid B.; Rossi, G. Victor; Goldstein, Frederick J. Dept. of Biological Sciences, Philadelphia College of Pharmacy and Science, Philadelphia, PA 19104 **Doxepin and imipramine: effect on catecholamine inhibition of ganglionic transmission.** Life Sciences (Oxford). 17(2):257-262, 1975.

The effects of doxepin (DOX) and imipramine (IM) on electrically evoked postganglionic potentials in the superior cervical ganglion were studied in the cat. Dose - response relationships indicated no significant difference between DOX and IM with regard to their effect on norepinephrine (NE) activity. Potentiation of dopamine (DA) induces suppression of ganglionic transmission by DOX and IM (25, 40 and 60 microg/kg) was not as pronounced as the potentiation of NE activity by these two antidepressants. Significant potentiation of DA was evident only at the 40 and 60 microg/kg dose levels of DOX and IM. Dose - response relationships indicate that potentiation of DA by DOX was significantly greater than that produced by IM. 17 references. (Author abstract modified)

225078 Grota, Lee J. Dept. of Psychiatry, University of Rochester School of Medicine and Dentistry, 260 Crittenden Blvd., Rochester, NY 14642 **Effects of early experience and dexamethasone on adrenocortical reactivity.** Developmental Psychobiology. 8(3):251-259, 1975.

The hypothesis that changes in circulating adrenocortical hormones (AH) mediate the long-term effects of shock in infant rats was tested. Dexamethasone (DM) administered through the mothers' milk was used to block adrenocortical responses to peripheral shock stimulation by the young. Control experiments indicate that the DM was present in the pups as early as 2 days after the mothers began drinking water containing the drug. Shock reduced adrenocrotical reactivity under conditions where the mother and the young were capable of an adrenocortical response to the shock, where either the mother or the young could have a response, and where neither the mother nor the young could have an adrenocortical response to this early stimulation. The data do not support the hypothesis that a pituitary - adrenocortical response of either the mother or the young mediates the effects of stimulation in infancy on subsequent adrenocortical reactivity. 28 references. (Author abstract modified)

225166 Hanson, Harley M. Merck Institute for Therapeutic Research, West Point, PA 19486 **Psychophysical evaluation of toxic effects on sensory systems.** Federation Proceedings. 34(9):1852-1857, 1975.

Psychophysical evaluation of toxic effects on sensory systems is illustrated using behavioral methods for four compounds affecting either the visual or auditory systems. Sodium salicylate and kanamycin, both reported to produce hearing deficits in man, have also been demonstrated to affect auditory thresholds in monkeys. With the latter drug the deficits measured were found to be correlated with specific loss of receptor cells in the cochlea. Pheniprazine, known to induce red - green color blindness, disrupted a wavelength discrimination in pigeons. Trans 11-amino-10,11-dihydro-5-(3-dimethyl aminopropyl)-5,10-epoxy-5H-dibenzo-(a,d)-cycloheptene dihydrochloride, which was found to bleach the tapidum lucidum in dogs when given subacutely, was found to decrease sensitivity to light. The loss in sensitivity measured by behavioral techniques was not correlated with the loss of coloration of the tapidum. Monkeys, not having a tapidum, did not show a similar effect. 7 references. (Author abstract modified)

225307 Zivkovic, B.; Guidotti, A.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC **Role for post-synaptic dopamine receptors in the regulation of the kinetic state of striatal tyrosine hydroxylase. (Unpublished paper).** Washington, DC, NIMH, 1975. 8 p.

Effects of antipsychotics on the kinetic state of brain tyrosine hydroxylase (TH) in areas innervated by dopamine (DA) neurons were studied in rats. In rats injected with haloperidol, findings indicate that the kinetic activity of striatal TH for the pteridine cofactor is lowered independently from a blockade of DA autoreceptors. Data suggest that haloperidol and other antipsychotics regulate the kinetic state of striatal TH by blocking the postsynaptic DA receptor, thereby activating DA neurons through a change in the function of the feedback regulatory neuronal loop linking striatum to substantia nigra. 14 references.

225527 Yanai, Joseph; Sze, Paul Y.; Ginsburg, Benson E. Department of Biobehavioral Sciences, University of Connecticut, Storrs, CT 06268 **Effects of aminergic drugs and glutamic acid on audiogenic seizures induced by early exposure to ethanol.** Epilepsia (Amsterdam). 16(1):67-71, 1975.

Adult inbred C57BL/10/Bg mice, normally resistant to audiogenic seizures, became susceptible when the mothers drank 10% ethanol in water during pregnancy and for 14 days postpartum. Reserpine enhanced the incidence of seizures, and the effect was reversed by 5-hydroxytryptophan but not by dihydroxyphenylalanine. p-Chlorophenylalanine also enhanced the incidence of seizures, whereas alpha-methyl-p-tyrosine had no effect. Monosodium glutamate almost completely prevented seizures. These results are consistent with the interpretation that the serotonergic systems may be among those involved in the seizure mechanism induced by fetal and early exposure to ethanol. 26 references. (Author abstract)

225558 Constantinidis, J.; Geissbuhler, F.; Gaillard, J. M.; Aubert, C.; Hovaguimian, Th.; Tissot, R. Clinique psychiatrique universitaire de Geneve, CH-1225 Chene Bourg, Geneva, Switzerland /**Formation of norepinephrine in the brain of rats after administration of (+)-erythro-3,4-dihydroxyphenyl-**

serine./ Formation de noradrenaline dans le cerveau du rat apres administration de (+)-erythro-3,4-dihydroxyphenylserine. Psychopharmacologia (Berlin). 41(3):201-209, 1975.

In a fluorescence microscopy study of rat brains after administrating (+)-erythro-dihydroxyphenylserine (DOPS), (+)-erythro-DOPS induced an increase of brain norepinephrine (NE), part of which was formed in the capillary walls. A slight diminution of this increase resulted when (+)-erythro-DOPS was administered after inhibition of peripheral decarboxylase. It is suggested that this might be the result of the algebraic sum of two inversely acting processes: suppression of NE synthesis in capillary walls and enhancement of parenchymatous NE in some brain areas. (+)-erythro-DOPS enters different brain structures nonspecifically and NE is formed in DA and 5-HT systems, displacing the amines. Results indicate that the NE formed by (+)-erythro-DOPS in NE systems is rapidly catabolized. Possible pharmacological effects are discussed. 19 references. (Author abstract modified)

225562 Wauquier, Albert; Niemegeers, Carlos J. E.; Lal, Harbans. Janssen Pharmaceutica, Research Laboratoria, B-2340 Beerse, Belgium **Differential antagonism by the anticholinergic dexetimide of inhibitory effects of haloperidol and fentanyl on brain self-stimulation.** Psychopharmacologia (Berlin). 41(3):229-235, 1975.

Haloperiodol or fentanyl injected subcutaneously suppressed bar pressing for brain simulation in rats implanted with electrodes in the lateral hypothalamic area of the medial forebrain bundle. Increasing doses of the central anticholinergic dexetimide gradually antagonized the haloperiodol effects. The highest dose of dexetimide did not reduce the fentanyl induced inhibition. The results, together with a literature survey on the anticholinergic effects on neuroleptic induced catalepsy and inhibition of avoidance behavior, are related to biochemical findings and clinical effects. 54 references. (Author abstract)

225565 Nielsen, M.; Eplov, L.; Scheel-Kruger, J. Sct. Hans Hospital, Dept E, DK-4000 Roskilde, Denmark **The effect of amitriptyline, desipramine and imipramine on the in vivo brain synthesis of 3H-noradrenaline from 3H-L-dopa in the rat.** Psychopharmacologia (Berlin). 41(3):249-254, 1975.

The effect of amitriptyline, desipramine, and imipramine on the in vivo brain synthesis of 3H-noradrenaline from 3H-L-dopa was experimentally studied. 3H-L-dopa was given to rats after a peripheral decarboxylase inhibitor Ro 4-4602, and the effect of 30 minutes pretreatment with amitriptyline, desipramine, and imipramine on the brain formation of 3H-dopamine, 3H-noradrenaline, and their major metabolites was investigated. Findings indicate that desipramine and imipramine inhibit the 3H-noradrenaline biosynthesis from 3H-L-dopa, an effect related to the membrane inhibitory effect. The mechanism of action was not determined. 36 references. (Author abstract modified)

225567 Phillips, Keith C.; Wray, Samuel R. Dept. of Psychology, University of Hull, England **Failure of antiserotonergic agents to modify levallorphan-induced sterotypy in rats.** Psychopharmacologia (Berlin). 41(3):263-265, 1975.

To explore the possibility that the stereotypic behavior induced by levallorphan, a narcotic antagonist, might be influenced by a serotonergic system, two antiserotonergic agents, methysergide and parachlorophenylalanine, were administered to rats. That they failed to modify such sterotypy was thought to imply that serotonin is not involved in the process. It is suggested that dopamine might be the principal mediator in the stereotypic behavior. 20 references. (Author abstract modified)

04 MECHANISM OF ACTION: BEHAVIORAL

213422 Kovacs, Gabor L.; Telegdy, Gyula; Lissak, Kalman. Department of Physiology, University Medical School, Pecs, Hungary **The role of monoamines in avoidance behaviour in rats.** Brain Research (Amsterdam). 85(1):198-199, 1975.

At the 6th annual meeting of the European Brain and Behaviour Society, a study of the role of monoamines in avoidance behavior in rats was presented. Monoamine oxidase inhibitor treatment facilitated the extinction of the active avoidance reflex p-Chlorophenylalanine (PCPA) given every 72 h. caused a transient decrease in the rate of extinction in the first 2 days following injection; however, the tendency to extinction remained unaffected. Alpha-methyl-p-tyrosine-methylester (MT) facilitated the extinction. PCPA pretreatment was able to counteract the nialamide induced facilitation of extinction; MT in combination with nialamide resulted in the same effect as nialamide alone. Nialamide lengthened the latency to avoidance reaction. PCPA shortened the latency, while MT had no effect. PCPA or MT in combination with nialamide blocked the nialamide induced action on latency of passive avoidance reflex. The results indicate that catecholamines and serotonin are involved in the neural control of extinction of active reflex and passive avoidance behavior. It seems that there is some difference in the involvement of catecholamines and serotonin in the regulation of these behavioral patterns. Increased levels of serotonin or decreased levels of brain catecholamines facilitate the extinction of active avoidance behavior, while in the passive avoidance reflex situation, increased levels of serotonin and catecholamines both lengthen the latency of passive avoidance reflex. (Journal abstract modified)

213431 Stinus, L.; Cardo, B. Laboratoire de Psychophysiologie, Universite de Bordeaux I, 33405 Talence, France **Effect of various inhibitors of tyrosine hydroxylase and dopamine beta- hydroxylase on self-stimulation behaviour.** Brain Research (Amsterdam). 85(1):196, 1975.

At the 6th annual meeting of the European Brain and Behaviour Society, a study of the behavioral effects of low doses of the catecholamine (CA) synthesis inhibitor, alpha-methyl-p-tyrosine (MpT) or the norepinephrine (NE) synthesis inhibitors in rats pretreated with reserpine 24 h before was presented. Rats were implanted either in the area ventralis tegmenti (ACT) or in lateral hypothalamus (LH). The modifications of CA synthesis and endogenous levels of central monoamines induced by these pharmacological treatments were estimated in a parallel experiment. Reserpine treatment produced a slow decrease of self-stimulation (SS) rates during the first 12 h; SS rates were 85% of control values 24 h after reserpine injection. MpT injection in reserpine pretreated rats inhibited Ss whereas dopamine beta-hydroxylase (DBH) inhibitors had no effect on SS. Dopamine (DA) synthesis was not reduced whereas NE synthesis was reduced to 58% 24 h after reserpine, MpT produced a severe decrease of CA synthesis to 23% of control level (either in DA or NE neurones), whereas the DBH inhibitors produced a complete blockade of NE synthesis associated with a parallel increase in DA synthesis (205%). The major conclusion is that a dopaminergic system seems to be involved in SS, either in the AVT or in the LH. Probably the same system is involved at these two levels. (Journal abstract modified)

213432 Kelly, P. H. Department of Experimental Psychology, University of Cambridge Cambridge, England **Enhancement of self-stimulation by Deprenil: evidence for a role of dopamine neurones in reward.** Brain Research (Amsterdam). 85(1):196-197, 1975.

At the 6th annual meeting of the European Brain and Behaviour Society, a study of enhancement of self-stimulation by Deprenil was presented. It was shown that Deprenil produces a marked enhancement of self-stimulation. The enhanced response was not stereotyped pressing because the animals rapidly stopped responding if the stimulation was turned off. This enhancement is evidence that activation of dopamine neurones can produce reward. It is proposed that Deprenil enhances self-stimulation by inhibiting the breakdown of dopamine released by the stimulation. The weak inhibitory action of Deprenil on noradernaline uptake is probably not involved in its effect on self-stimulation, since the more potent uptake inhibitor, imipramine, does not facilitate self-stimulation. Rather the enhancement of self-stimulation produced by Deprenil is evidence that activation of dopamine neurones can produce reward. 2 references. (Journal abstract modified)

213434 Asberg, H.; Soderberg, U. Neurophysiological Laboratory, Ulleraker Hospital, S-750 17 Uppsala, Sweden **Thyroxine-like effects of zinc on brain and behaviour with firm dependence on several hormones.** Brain Research (Amsterdam). 85(1):197-198, 1975.

At the 6th annual meeting of the European Brain and Behaviour Society, a study of thyroxine like effects of zinc on brain and behavior with firm dependence on several hormones was presented. Serum, brain and muscle zinc levels were measured in intact male and female Sprague-Dawley and Wistar rats, after thyroid and/or gonadectomy, and after heat exposure. Normal and zinc supplemented food and water were used. Intact male rats had higher serum zinc levels than female and castrated male rats, but total brain zinc concentration was much higher in females than in males. Radiothyroidectomy reduced serum zinc level by 20%. Thyroxine restored serum levels. Hypothyroidism slowly reduced brain zinc level. Heat exposure exaggerated the effects of thyroidectomy. In all groups 50% of animals received extra zinc for 1 month. An open field test then revealed that zinc treatment increased locomotion and rearing scores. Food intake was raised, particularly in relation to weight gain, a sign of increased activity level. Zinc also eliminated the heat induced polydipsia of hypothyroid rats. 1 reference. (Journal abstract modified)

213469 Aleksidze, N. G.; Meshvelishvili, D. F.; Balavadze, M. V. no address /**On the participation of biogenic amines and their synthetic enzymes in the mechanisms of image memory.**/ Ob uchastii biogennykh aminov i fermentov ikh prevrashcheniya v mekhanizmakh obraznoy pamyati. Soobshcheniya akademii nauk gruzinskoy SSR (Tbilisi). 76(1):157-160, 1974.

The psychoneural behavior of rats and the exchange of biogenic amines during differential inhibition of subcortical white matter cholinesterase (ChE) and monoamine oxidase (MAO) were investigated. ChE and MAO activity were determined spectrophotometrically; catecholamine and serotonin content were measured by thin layer chromatography. The rats' memory was evaluated by their free behavior in T-maze. Interperitonal injection of both physostigmine and hyperazide led to memory deterioration. Acetylcholine, ChE and MAO were found to be components of a complex functional system. Disturbance of the integrity of these components was concluded to cause the deterioration of image memory. 14 references. (Journal abstract modified)

213491 Lokhov, M. I.; Gal'dinov, G. V. Laboratoriya fiziologicheskikh mekhanizmov upravleniya pamyat'yu, Instituta eksperimental'noy meditsiny AMN SSSR, Leningrad /**On the physiological mechanisms of the influence of phenamine and micropolarization on long-term memory processes.**/ O fiziologicheskikh mekhanizmakh vozdeystviya fenamina i mikropolyarizatsii na protsessy dolgosrochnoy paymati. Fizologicheskiy zhurnal SSSR imeni I. M. Sechenova (Leningrad). 60(10):1494-1500, 1974.

The physiological mechanisms of the influence of phenamine and micropolarization on long-term memory processes were investigated in chronic experiments in cats. Small doses of phenamine combined with electrical stimulation of the temporal and motor cortices were found similar to the effect of direct micropolarization of the brain in the accleration of the formation of long-term memory traces during motor and time responses. The effect was attributed to the controlling effect of phenamine on the brain activating arousal systems. Restoration of trace reproduction after preliminary extinguishing was attributed to optimal micropolarization of both the cortical foci of learning and the posterior hypothalamus or midbrain reticular formation. Reproduction realization on the basis of triggering by specific signal of the trace selection mechanisms was hypothesized. 12 references. (Journal abstract modified)

213528 Beaton, John M.; Smythies, John R.; Bradley, Ronald J. Department of Psychiatry, University of Alabama, Birmingham, AL **The behavioral effects of L-methionine and related compounds in rats and mice.** Biological Psychiatry. 10(1):45-52, 1975.

The effects of L-methionine, betaine (another methyl group donor), L-methionine plus L-serine, L-cysteine, L-serine, and saline (as a control) were studied on the sleep - wake cycles of random bred Swiss mice and on the avoidance behavior of rats. L-methionine plus L-histidine, L-methionine plus nicotinamide, L-histidine, and nicotinamide were also tested in the mice. Daily injections of 250mg/kg of these compounds were administered for at least 21 consecutive days. Schedule performance in the rat and the sleep - wake cycles of the mice were monitored during this period and compared to controls. L-Methionine induced behavioral and sleep cycle disturbances which were removed by the simultaneous administration of L-serine but not by the addition of L-histidine or nicotinamide. These data suggest that the disruption may be due to an increase in the levels of one of the metabolites of methionine, homocysteine, rather than to an increase in the number of available methyl groups. 10 references. (Author abstract modified)

213531 Ellinwood, Everett H., Jr.; Kilbey, M. Marlyne. Department of Psychiatry, Duke University Medical Center, Durham, NC **Amphetamine stereotypy: the influence of environmental factors and prepotent behavioral patterns on its topography and development.** Biological Psychiatry. 10(1):3-16, 1975.

A strong contribution of the behavioral pattern manifested at the time of initial amphetamine injection to the topography and development of the stereotypy that develops with chronic amphetamine intoxication is reported. These initial behavioral patterns reflect learned behaviors, species specific behaviors, behaviors associated with amphetamine arousal, and novel behaviors reflecting unique environmental circumstances prevailing at the time of administration. In an experiment using eight dogs administered amphetamine in a situation which allowed interaction between the animals, the behavioral stereotypies that developed were comprised of the social in-

teraction patterns ongoing at the time of initial drug effects. Experiments with rats have demonstrated that the configuration of the enclosure in which they are injected influences the initial behavioral reactions to amphetamine and thus modifies the stereotypy. Monkeys incorporate components of the initial behaviors associated with amphetamine administration into a wider range of stereotyped patterns over months of chronic intoxication, and eventually the stereotypy may evolve into a specific dyskinesia involving movements of the original behavioral component. 4 references. (Author abstract modified)

213590 Kjellberg, B.; Randrup, A. AB Ferrosan, Malmo, Sweden **Partial restoration by an a neuroleptic (Spiramide) of items of grooming behaviour supressed by amphetamine.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 210(1):61-66, 1974.

The differences between hind leg grooming and the other types of grooming behavior with respect to the amphetamine - neuroleptic antagonism were examined in the rat. The neuroleptic drug spiramide restored grooming behavior of rats suppressed by amphetamine. Since spiramide can be regarded as a specific blocker of dopamine, the experiments indicate that dopaminergic systems in the brain affect grooming behavior. The restoration of grooming was not complete, grooming with the hind leg being particularly difficult to restore and more difficult the higher the amphetamine dose. Possible causes for the incompleteness of the restoration are discussed, and also possible relations of these findings with the incomplete normalization of psychotic patients treated with neuroleptic drugs. 19 references. (Author abstract)

213592 Sanghvi, I.; Gershon, S. Neuropsychopharmacology Research Unit, Department of Psychiatry, New York University Medical Center, New York, NY 10016 **Yohimbine: behavioral and biochemical effects in mice.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 210(1):108-120, 1974.

The acute effect of yohimbine, an indole alkaloid, was investigated on the spontaneous motor activity, temperature, and brain serotonin metabolism in mice. The behavioral effects of yohimbine were compared with those of reserpine. Yohimbine and reserpine decreased the spontaneous motor activity. 5-Hydroxytryptophan also decreased the motor activity and was synergistic with yohimbine. Monoamine oxidase inhibitors partially antagonized the yohimbine effect. Depletion of catecholamine stores by alpha-methyl-metatyrosine or inhibition of their synthesis by alpha-methyl-para-tyrosine accentuated the behavioral effects of yohimbine. Methysergide, a serotonin antagonist, initially antagonized, but later prolonged, the effects of yohimbine. It is suggested that, following acute administration, the behavioral effect of yohimbine is due to its effect on catecholamine metabolism and possibly to a direct stimulation of serotonin receptors in the brain. Chronically, yohimbine may produce its effects by promoting increased synthesis of serotonin. 22 references. (Author abstract modified)

213612 Heise, George A. Indiana University, Bloomington, IN 47401 **Program in behavioral pharmacology.** Psychopharmacology Bulletin. 11(2):47, 1975.

The specific effects of drugs on stimulus discrimination, memory, and learning are being explored, concentrating on scopolamine, atropine, and d-amphetamine, compounds that alter the functioning of the putative central cholinergic and noradrenergic transmitter systems. Scopolamine does not disinhibit performance when there is no delay between stimulus presentation and the occurrence of the response. It is suggested that effects of drugs on performance in delayed response experiments should be attributed to changes in registration and retrieval of discrimination events rather than their storage.

213619 McKearney, James W. Worcester Foundation for Experimental Biology, Shrewsbury, MA **Drug effects on behavior maintained by aversive events.** Psychopharmacology Bulletin. 11(2):52-53, 1975.

The ways in which the behavioral effects of drugs depend on the details of the control of the behavior by the environment are being studied in squirrel monkeys and pigeons. The main focus is on behavior under control of events usually thought to be aversive. Many of the experiments involve procedures in which the presentation of aversive stimuli maintains complex patterns of responding. Drug effects on these seemingly anomalous behaviors are compared with effects on behavior suppressed by punishment, with behavior maintained by termination or postponement of aversive events, and with responses maintained by such events as food presentation.

213622 Norton, Stata. University of Kansas Medical Center, Kansas City, MO **Psychoactive drugs and the organization of behavior.** Psychopharmacology Bulletin. 11(2):54-55, 1975.

Analysis of the kinds of behavior demonstrated by hyperactive subjects is presented, focusing on drug effects in subjects made hyperactive by lesions placed in the "hyperkinetic pathway", a region extending from the frontal cortex to the substantia nigra. Three models of hyperactive behavior in rats are proposed: one in which some behavioral acts are increased in frequency, a second in which the duration of some activities is decreased, and a third in which various acts are altered in the sequences in which they occur with time. Analysis of experimental trials indicates that the normal rat made hyperactive by amphetamine shows a combination of all three of these models.

213631 Seiden, Lewis S. University of Chicago, Chicago, IL 60637 **Brain monoamines and behavior.** Psychopharmacology Bulletin. 11(2):60-61, 1975.

Psychotropic drugs such as reserpine and LSD are being used to define the role of brain catecholamines in determining ongoing operant behavior. Neurochemical correlates of conditioned behavior are examined by measuring brain and tissue catecholamine levels; catecholamine turnover in the brain is determined after administration of amine depleting drugs. Behavioral changes are measured using a conditioned avoidance paradigm as well as operant schedules of positive reinforcement. Experiments using amphetamine in rats suggest the possibility that contingent tolerance to the anorexic effects of amphetamine is correlated with tolerance to its effects on norepinephrine metabolism in the brain. It is suggested that measurements of amine turnover might provide a better index for study than total levels of amines in the brain. Depletion of catecholamines by methyl-para-tyrosine disrupts fixed responding but not fixed interval responding.

213634 Werner, Gerhard. University of Pittsburgh, Pittsburgh, PA 15213 **Hallucinogenic drug action on the somatosensory system.** Psychopharmacology Bulletin. 11(2):63, 1975.

The correlation of behavioral effects of hallucinogenic drugs and their actions on central neural activity are being studied in rhesus monkeys. Preliminary experiments have been aimed at

establishing baseline data in the absence of drug action, which will constitute controls for the assessment of drug effects on behavioral performance and concomitant neural activity. Studies with behavior altering pharmacological agents, notably phencyclidine and chlorpromazine, will be conducted and compared with the baseline data.

213635 Winter, Jerrold C. State University of New York, Buffalo, NY 14222 **The behavioral pharmacology of psychoactive drugs.** Psychopharmacology Bulletin. 11(2):63-64, 1975.

The effects of psychoactive drugs upon operant behavior, and the mechanisms by which these effects are produced, are being studied in rats and monkeys. Pharmacologic and behavioral analyses of the stimulus properties of compounds such as barbiturates, ethanol, amphetamine, narcotic analgesics, and hallucinogens are expected to provide a new perspective on these agents and offer the possibility of preclinical identification of drugs likely to be abused ny humans. Results indicate that cellular or behavioral mechanisms may be important in the development of tolerance. LSD and mescaline appear to have at least one common site of action. The two compounds can serve as discriminative stimuli when either drug is paired with saline; the degree of discrimination varies with drug dose.

213853 Springer, Alan D.; Schoel, W. Michael; Klinger, Paul D.; Agranoff, Bernard W. Mental Health Research Institute, University of Michigan, Ann Arbor, MI 48104 **Anterograde and retrograde effects of electroconvulsive shock and of puromycin on memory formation in the goldfish.** Behavioral Biology. 13(4):467-481, 1975.

The possibility of electroconvulsive shock (ECS) induced anterograde amnesia was explored in a multitrial task in the goldfish, and the proactive effects of puromycin on memory were studied. ECS or puromycin administered prior to training did not significantly impair acquisition of shock avoidance. Significant retention deficits were observed on retraining 72 hours later in groups of fish that received ECS 2.5, 1 or 0.5hours before training as well as in groups that received ECS 0, 4, or 25 hours after training. Puromycin produces significant retention deficits on retraining when given 24, 16, 8, 4 or 0 hours prior to, or 0 or 0.25 hours following training. A temporal course of development of the retention deficit that has been seen with puromycin was not observed with ECS as the deficit was maximal at the earliest train - retrain interval examined. ECS administered before both training and retraining did not relieve the deficit. Since performance was not diminished in fish retrained just after ECS, it appears that this proactive effect of ECS reflects disruption of memory rather than state dependent learning. 21 references. (Author abstract modified)

214012 Jerussi, Thomas P.; Glick, Stanley D. Dept. of Pharmacology, Mount Sinai School of Medicine, 5th Ave. and 100 St., New York, NY 10029 **Apomorphine-induced rotation in normal rats and interaction with unilateral caudate lesions.** Psyphopharmacologia (Berlin). 40(4):329-334, 1975.

Apomorphine induced rotational behavior in normal unoperated rats was studied. This rotation increased with increasing dose up to 10.0mg/kg, after which the dose response curve appeared to plateau. Although there was large variability among rats, rotation for each rat was consistent in both direction and magnitude from week to week. Rotation was not antagonized by alpha-methylpara-tyrosine. When rats with unilateral lesions of the caudate nucleus were tested with apomorphine, postoperative rotation was significantly influenced by the direction of preoperative rotation; rats rotated more postoperatively if the lesion was made ipsilateral rather than contralateral to their preoperative direction of rotation. These results suggest that there is a bilateral asymmetry of dopaminergic receptors in the nigro-striatal pathways of normal rats. 18 references. (Author abstract)

214013 Barrett, James E.; Weinberg, Elizabeth S. Department of Psychology, University of Maryland, College Park, MD 20742 **Effects of chlordiazepoxide on schedule-induced water and alcohol consumption in the squirrel monkey.** Psychopharmacologia (Berlin). 40(4):319-328, 1975.

The effects of chlordiazepoxide on schedule induced water and alcohol consumption in the squirrel monkey were examined. Lever pressing of five squirrel monkeys was maintained by a 3 min fixed-interval schedule of food presentation. Three monkeys had water concurrently available and, for a second pair of monkeys, initially water, then increasing concentrations of alcohol were present. Substantial amounts of postpellet drinking occurred with all five monkeys. The amount of water ingested was approximately 100 ml per session, that of 3% alcohol nearly 63 ml. For the monkeys drinking alcohol, increasing concentrations of alcohol decreased both the rate of lever pressing and the volume of fluid consumed. Chlordiazepoxide produced increases in lever pressing and in the schedule induced consumption of both 3% alcohol and water. 23 references. (Author abstract)

214014 Kallman, W. M.; Isaac, W. Department of Psychology, University of Georgia, Athens, GA 30602 **The effects of age and illumination on the dose-response curves for three stimulants.** Psychopharmacologia (Berlin). 40(4):313-318, 1975.

The dose response relationships for three stimulants have been explored in the rat. These drugs have been shown to differ in potency and, with successive doubling of doses, have been found to have dose response curves of differing slopes. In addition, the relationship between dose and activity level was not the same for younger and older rats. The relationship between dosage of both d-amphetamine and methylphenidate and locomotor activity was not the same in the light and the dark. The latter finding suggests a difference between these two stimulants and the third stimulant studied, caffeine, whose effects were unaltered by ambient illumination level. 14 references. (Author abstract)

214016 Cox, T.; Tye, N. Department of Psychology, University of Nottingham, Nottingham NG7 2RD, England **The effects of amphetamine, imipramine and ICI 58,834 (Vivalan), a potential antidepressant, on unconditioned behaviour in rats.** Psychopharmacologia (Berlin). 40(4):297-304, 1975.

The effects of amphetamine, imipramine and ICI 58,834 (Vivlaan), on the unconditioned behaviour of rats were compared using a novelty preference test and the open field test. Overall, the effects of ICI 58,834 showed a marked resemblance to those of imipramine but differed from those of amphetamine. It is suggested that an adequate explanation of these drugs' effects can be offered in terms of changes in emotional reactivity, in general activity, and in exploratory activity. A dissociation of drug effects on general and exploratory activity in the novelty preference test was demonstrated. The use of this test and the open field test in drug screening is briefly discussed. 19 references. (Author abstract)

214017 Sofia, R. Duane; Vassar, Heidi B.; Knobloch, Linda C. Wallace Laboratories, Department of Pharmacology and Toxicology, Cranbury, NJ 08512 **Comparative analgesic activity**

of various naturally occurring cannabinoids in mice and rats. Psychopharmacologia (Berlin). 40(4):285-295, 1975.

The analgesic effectiveness of delta9-tetrahydrocannabinol (THC), a crude marihuana extract (CME), cannabinol (CBN), cannabidiol (CBD), morphine SO4 and aspirin following oral administration was directly compared in mice using the acetic induced writhing and hot plate tests and the Randall-Selitto paw pressure test in rats. THC and morphine were equipotent in all tests except that morphine was significantly more potent in elevating pain threshold in the uninflamed rat hind paw. In terms of THC content, CME was nearly equipotent in the hot plate and Randall-Selitto tests, but was three times more potent in the acetic acid writhing test. On the other hand, CBN, like aspirin, was only effective in reducing writhing frequency in mice and raising pain threshold of the inflamed paw of the rat (equipotent with aspirin). CBD did not display a significantly analgesic effect in any of the test systems used. The results of this investigation seem to suggest that both THC and CME possess narcotic like analgesic activity similar to morphine, while CBN appears to be a nonnarcotic type analgesic like aspirin. 30 references. (Author abstract)

214056 Hiebert, Linda M.; Jaques, L. B. Hemostasis-Thrombosis Research Unit, Dept. of Physiology, College of Medicine, Univ. of Saskatchewan, Saskatoon, Saskatchewan **Blocking of stress by pentobarbital-morphine as related to training and age of rats.** Steroids and Lipids Research (Basel). 5(4):255-261, 1974.

Blockage of reduction in adrenal ascorbic acid from stress in rats by the prior administration intraperitoneally of pentobarbital with morphine sulfate was examined. The influence of several variables on this phenomenon was studied with several stressors, shortening the time interval between pentobarbital - morphine and stressor. Results show that pentobarbital - morphine blocked the adrenal ascorbic acid depletion by stress when young trained rats were used. No block in adrenal ascorbic acid depletion occurred in untrained rats or in older trained rats. 17 references. (Author abstract modified)

214067 Segal, David S.; Callaghan, Maureen; Mandell, Arnold J. Dept. of Psychiatry, Univ. of California, San Diego, Medical School, La Jolla, CA 92037 **Alterations in behaviour and catecholamine biosynthesis induced by lithium.** Nature (London). 254(5495):58-59, 1975.

Alterations in behavior and catecholamine biosynthesis induced by lithium were examined in male rats which received injections of lithium choride. A control group was injected with saline. Spontaneous activity was monitored for 2 hours after the final injection, then rats were administered amphetamine sulfate, and activity was measured for another 2 hours. Amphetamine produced a moderate increase in locomotion which was suppressed 3040% over controls in lithium pretreated groups. Tolerance to the suppressive effect occurred after 8 days. Homogenates of four regions of the rats' brains were examined for tyrosine hydroxylase (TH) activity and alterations were found only in the dopamingergic system, where TH activity was increased. Results are compared with the findings of previous studies, and it is concluded that the observed augmentation of TH activity by lithium may represent a compensatory response to the lithium induced impairment of catecholamine transmission which partially counteracts the effects of lithium on behavior. 35 references.

214205 Marriott, John Gibson. University of Colorado **Adrenergic and cholinergic drug effects upon short-term memory in mice. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-3806 HC$13.50 MF$5.00 113 p.

Three experiments investigated methodological and conceptual problems associated with the study of biological bases of short-term memory (STM) in mice. Focus was on the role of putative synaptic transmitter substances in memory and the effects of pharmacological manipulations of neurohumoral systems upon learned behaviors. In experiment one, inbred strains were trained in a T-maze on a serial position reversal task until they acquired the successive reversal learning set. They were then tested for retention of the reversal cue after delays of 0, 20, 15, 30, and 60 min. Adrenergic contributions to STM were further assessed in experiment two by administering the tyrosine hydroxylase inhibitor, diethyldithiocarbamate. Experiment three examined the dose response relationships of the drugs studied in experiment two. Results indicate that cholinergic, but not adrenergic, mechanisms are necessary for the normal expression of STM. Drugs which impair cholinergic functioning produce disruption of retention. Drugs which impair adrenergic functioning have no effects upon memory, although effects upon performance are evident. Findings suggest the cholinergic synapse as the locus of mechanisms responsible for the elaboration of STM in mice. (Journal abstract modified)

214206 Ritter, Robert Clinton. University of Pennsylvania **Noradrenergic control of spontaneous meal size in the rat. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-2769 HC$13.00 MF$5.00 82 p.

The effect of low doses of norepinephrine (NE) on the parameters of spontaneous ingestive behavior was examined in rats. Infusions of NE, at doses which nearly triple meal size, did not elicit eating when made during an intermeal interval. Multiple infusions of the alpha-noradrenergic receptor blocking agent, phentolamine, at a dose of 29.0nanomoles per infusion decreased meal size but did not decrease meal frequency. Propranolol 67.8nanomoles had no effect on meal size or frequency. Intrahypothalamic infusion of protriptyline, a drug which blocks the physiological inactivation of NE, enhanced food intake after 13 hr but not after only 1 hr food deprivation. All cannula placements studied were in the anterior diencephalon. However, trajectories consistently passed through the cerebral ventricles. Overall results show that NE increases food intake at doses less than 1% of the brain's normal NE content. Meal size is more susceptible to alteration by NE manipulations than meal frequency. The brain's own NE system may function to sustain food intake once feeding is initiated. This function of brain NE may exert control on spontaneous meal size. (Journal abstract modified)

214207 Spencer, John William. University of Oklahoma **A comparison between caudate, amygdaloid and hypothalamic self stimulation in squirrel monkeys (Saimiri sciureus). (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-2986 HC$13.50 MF$5.00 211 p.

The effects of caudate, amygdaloid and hypothalamic self-stimulation in squirrel monkeys (Saimiri sciureus) were compared in Ss implanted with electrodes in the head of the caudate nucleus, medial forebrain bundle (MFB), and anterior lateral and central amygdalar nuclei. These sites were specifically compared regarding their support of intracranial self-stimulation (ICSS). The effects of low, moderate, and high doses of amphetamine, chlorpromazine (CPZ), and clonidine (a drug which stimulates central norepinephrine receptors without influencing dopamine or serotonin receptors) were also ex-

amined. Findings suggest that: (1) consistent rates of ICSS can be obtained from broad regions of the squirrel monkey brain and rate of ICSS from certain amygdalar nuclei may be influenced by the elicitation of other underlying responses; (2) the dose effects of amphetamine and CPZ on ICSS are not only observed within the hypothalamus, but are extensive throughout the brain, involving telencephalic, as well as diencephalic structures; (3) since hypothalamus, but not caudate, ICSS can be blocked by drugs which have select sites of action, other pathways besides the MFB may also support ICSS. (Journal abstract modified)

215063 Krsiak, M. Institute of Pharmacology, Czechoslovak Academy of Sciences, Albertov 4, 128 00 Prague 2 **Isolation-induced timidity in mice as a measure of anxiolytic activity of drugs.** Activitas Nervosa Superior (Praha). 16(4):241-242, 1974.

At the 16th Annual Psychopharmacological Meeting, Jesenik, 1974, a paper was presented in which the effects of some psychotropic drugs on isolation induced timidity in mice were examined. The results of studies with male albinos suggest that drugs reducing anxiety in man (e.g.,barbital, chlordiazepooxide, diazepam, and chlorpromazine) inhibit the isolation induced timidity without producing general sedation. Imipramine, d-amphetamine, and LSD, which have no anxiolytic effect in man, did not inhibit selectively the timid response. The timidity shown by some singly housed male mice on interaction with nonaggressive group housed partners is concluded to be a good measure of the anxiolytic activity of drugs. 4 references.

215067 Frankova, S.; Jakoubek, B. Institute of Clinical and Experimental Medicine, Prague **Long term behavioural effects of diazepam and ACTH, administered early in life.** Activitas Nervosa Superior (Praha). 16(4):247-249, 1974.

At the 16th Annual Psychopharmacological Meeting, Jesenik, 1974, a paper was presented which described the long-term behavioral effects of diazepam and adrenocorticotropic hormone (ACTH), administered daily between the second and twelfth day of life to male rat pups. Observations were made of rearing, motor disturbances (e.g.,sudden freezing, tremor, stereotypes, chaotic movements, displacement reactions), and contacts with objects (e.g.,sniffing, manipulation, biting). The results indicate a long-term effect of the drugs administered during the critical developmental stages.

215068 Lat, J.; Jakoubek, B. Institute of Physiology, Czechoslovak Academy of Sciences, Prague-Krc, Czechoslovakia 1083 **Permanent effects of repeated administration of ACTH and diazepam in early postnatal period upon the dynamics of excitation and inhibition during habituation.** Activitas Nervosa Superior (Praha). 16(4):249-250, 1974.

At the 16th Annual Psychopharmacological Meeting, Jesenik, 1974, a paper was presented in which the late effects of early daily treatments of adrenocorticotropic hormone (ACTH) and diazepam on adult male rats (age 4 mo) were described. Four parameters of activation and disactivation were selected: the level of maximum excitement; the time to reach maximum excitement; the rate of habituation; and the size of oscillations. The excitement was provoked by exposing the rats to a new environment for 8 min and the frequency of grid crossing and rearing reactions served as the dependent variable. The results indicate that: (1) all four parameters were attained; (2) ACTH and diazepam treatment in the first 12 days of life caused permanent changes in the dynamics of activation and disactivation; and (3) all substances affected the equilibrium between excitatory and inhibitory processes, especially diazepam. 3 references.

215487 Krauz, V. A. Otdel farmakologii, Instituta eksperimental'noy meditsiny AMN SSSR, Leningrad **/The correlation between the ventral and dorsal hippocampus during improvement or deterioration of short-term memory./** Vzaimootnosheniye mezhdu ventral'nym i dorzal'nym gippokampom pri uluchshenii i ukhudshenii kratkosrochnoy pamyati. Zhurnal vysshey nervnoy deyatel'nosti imeni I. P. Pavlova (Moskva). 24(1):33-41, 1974.

The functional state of the ventral hippocampus and its relationship to the dorsal hippocampus was investigated in dogs during changes in short-term memory ability elicited by various neurotropic drugs and electrical stimulation. Phenamine, ethymisol, strychnine and galantamine prolonged the maximum time of delayed reactions, which was used as a test for short-term memory. Methamysil, atropine, chlorpromazine and reserpine disturbed memory ability. Memory improvement induced by neurotropic drugs was caused by a higher ventral hippocampus excitability level and a lowered dorsal hippocampus excitability level. Memory improvement induced by ventral hippocampus electrical stimulation was accompanied by a decreased dorsal hippocampus excitability level. Memory deterioration caused by dorsal hippocampus stimulation was characterized by enhanced ventral hippocampus excitability. The different functional states of the ventral and dorsal hippocampus in the memory processes were tentatively concluded to be caused by dissimilar relationships between these formations and the mesencephalic reticular formation. 32 references. (Journal abstract modified)

215497 Vorob'yeva, T. M. Khar'kovskogo nauchno-issledovatel'skogo instituta nevrologii i psikhiatrii, Kharkov, U.S.S.R. **/A neuropharmacological analysis of cholinergic mechanisms of self-stimulation reactions./** Neyrofarmakologicheskiy analiz kholinergicheskikh mekhanizmov reaktsii samorazdrazheniya. Zhurnal vysshey nervnoy deyatel'nosti imeni I. P. Pavlova (Moskva). 24(1):172-180, 1974.

The effect of cholinomimetics and cholinolytics on posterior hypothalamic self-stimulation was investigated in 32 rats. Eserine and acetylcholine considerably inhibited, while atropine, amizyl and pentamine activated, the self-stimulation reaction following both parenteral and intracentral injections into the Old's emotiogenic zones. Cholinomimetic microinjections in the hippocampus inhibited posterior hypothalamic self-stimulation. The cholinergic mechanisms were concluded to function as an inhibitory link in the self-stimulation reaction. The hippocampal apparatus controlling the reaction was concluded to achieve its inhibitory and modualting effects by means of its own cholinergic mechanisms. 35 references. (Journal abstract modified)

215498 Shumilova, N. Ye. Meditsinskogo instituta, Kemerovo, U.S.S.R. **/Toward the question of the influence of sitmulation of the thalamic associative nuclei on the behavior of cats./** K voprosu o vliyanii razdrazheniya assotsiativnykh yader talamusa na povedeniye koshek. Zhurnal vysshey nervnoy deyatel'nosti imeni I. P. Pavlova (Moskva). 24(1):186-188, 1974.

The influence of acetylcholine, noradrenaline and electrical stimulation of the mediodorsal (MD), and rear lateral (RL), thalamic associative nuclei was investigated in cats. Acetylcholine injections had no visible effect on behavioral activity; noradrenaline injections caused a temporary disappearance of conditioned reflexes. The difference in drug effect was thought to be related to the difference in the sensitivity of the synpases of the thalamic neurons to the substances in-

volved. Weak electrical stimulation of the thalamic associative nuclei produced no visible changes; a strong electrical current eliminated conditioned reflex reactions. The effect of the current was attributed to excitation distribution over the general neuron ensemble and to the development of new functional correlations. 9 references.

215665 Bucci, Luigi. Laboratorio di Psicofarmacologia e Psicobiologia, Via Reno 1, Roma, Italy **The biphasic effect of small doses of tranylcypromine on the spontaneous motor activity and learned conditioned behaviour in rats.** Pharmacology (Basel). 12(6):354-361, 1974.

In a study of rats, tranylcypromine (TCP), a monoamine oxidase inhibitor with amphetamine like property, had at first a depressant effect and 5 h later stimulating effect on spontaneous motor activity and learned conditioned behavior. This latter effect was demonstrated by means of a modified conditioned avoidance response schedule and a specific time schedule interval. While 'he depressant effect of tranlycypromine may be due to the initial increase of brain serotonin caused by this drug, its delayed stimulating effect is, very likely, related to norepinephrine brain increase occurring a few hours after TCP administration. 11 references. (Author abstract)

215682 Shintomi, K. Safety Research Laboratory, Tanabe Seiyaku Co., Ltd., Yodogawa-ku, Osaka, 532, Japan **Effects of psychotropic drugs on methamphetamine-induced behavioral excitation in grouped mice.** European Journal of Pharmacology (Amsterdam). 31(2):195-206, 1975.

The effects of psychotropic drugs on methamphetamine induced behavioral excitation in grouped mice. The effects of various drugs tested, according to the minimal effective doses which inhibited fighting behavior and hyperactive behavior respectively, were: haloperidol, clothiapine; perphenazine; thiothixene, chlorpromazine; diazepam; reserpine, and phenoxybenzamine. Major tranquilizers except rauwolfia alkaloids completely inhibited both types of excited behavior at low doses, as compared with the taming effects of the drugs on footshock induced fighting episodes in pairs of mice. Minor tranquilizers suppressed only fighting behavior, showing little effect on hyperactive behavior. None of the antidepressants, adrenergic blocking agents and other drugs showed antagonism to both types of excited behavior. None of the antidepressants, adrenergic blocking agents and other drugs showed antagonism to both types of excited behavior. The results indicate that this method may be useful for the evaluation of psychotropic drug effects in grouped mice. 31 references. (Author abstract modified)

215684 Shintomi, Keiichi; Yamamura, Michio. Safety Research Laboratory, Tanabe Seiyaku Co., Ltd., Kashima, Yodogawa-ku, Osaka, 532, Japan **Effects of penfluridol and other drugs on apomorphine-induced stereotyped behavior in monkeys.** European Journal of Pharmacology (Amsterdam). 31(2):273-280, 1975.

The effects of some drugs on apomorphine induced stereotyped behavior were studied in male cynomolgus monkeys. Apomorphine produced the dose dependent stereotyped behavior characterized mainly by continuous licking and biting, and repetitive movements of the hands, head and body in the monkeys. Penfluridol as well as haloperidol showed a clear antagonistic effect on the apomorphine induced stereotyped behavior, while chlorpromazine was less antagonistic than haloperidol. The antagonistic effect of penfluridol lasted longer than that of haloperidol. In provoking stereotyped behavior in monkeys, apomorphine probably acts directly on dopamine receptors in the extrapyramidal system, and penfluridol is suggested to act as a dopamine receptor blocker with a long action. 29 references. (Author abstract modified)

215685 Gauron, Eugene F.; Rowley, Vinton N. College of Medicine, University of Iowa, Iowa City, Iowa 52242 **Methlphenidate effects on avoidance learning at two ages in the rat.** European Journal of Pharmacology (Amsterdam). 31(2):347-350, 1975.

The effects of methylphenidate on avoidance learning at two ages were examined in albino rats. The major findings indicated that no significant difference in avoidance response acquisition was obtained in the comparison between drug and control groups. A dose effect was obtained in that the M4.5group made significantly more correct responses than the M1.5group. Animals drugged beginning at 87 days made significantly more correct responses than those drugged beginning at 47 days. 10 references. (Author abstract modified)

215689 Vonvoigtlander, P. F.; Losey, E. G.; Triezenberg, H. J. Research Laboratories, The Upjohn Company, Kalamazoo, MI 49001 **Increased sensitivity to dopaminergic agents after chronic neuroleptic treatment.** Journal of Pharmacology and Experimental Therapeutics. 193(1):88-94, 1975.

Male CF-1 mice treated for 14 days with diets containing haloperidol, thioridazine HCl and 4'-fluoro-4(4-(p-fluorophenyl)-4-methoxycyclohexyl-amino-butyrophenone HCl (U35,777A) were examined for spontaneous and d-amphetamine stimulated motor activity. Two days after cessation of treatment, the mice displayed enhanced spontaneous and d-amphetamine stimulated motor activity. This effect was no longer apparent 9 days after neuroleptic intake was terminated. With a quantal test based on the climbing activity induced by apomorphine, it was determined that mice were also supersensitive to apomorphine at 2 days but not 9 days after withdrawal from chronic haloperidol. Chronic treatment with neuroleptics results in a brief supersensitivity to dopaminergic agents. This effect does not appear to be accompanied by increases in dopamine stimulated adenyl cyclase activity in the corpus striatum. 18 references. (Author abstract modified)

215693 Melo, J. C.; Graeff, F. G. Department of Pharmacology, Institute of Biological Sciences, Goiania, Goias, Brazil **Effect of intracerebroventricular bradykinin and related peptides on rabbit operant behavior.** Journal of Pharmacology and Experimental Therapeutics. 193(1):1-10, 1975.

The dose effect relationships of intraventricularly injected bradykinin, Gly-Arg-Met-Lys-bradykinin (GAML-bradykinin), synthetic substance P and angiotensin II on lever-lifting behavior of rabbits in a variable interval (VI) 72 second schedule of sweetened water presentation were determined. All peptides used caused dose dependent decreases in overall rates of VI responding during the experimental session. At the doses used, both bradykinin potentiating peptides caused uniform decreases in VI responding throughout the experimental session. Gross behavioral changes caused by peptides were also observed. After the intraventricular injection of bradykinin or GAML-bradykinin, rabbits showed decreased motility, ptosis, miosis and lowered ears; after angiotensin II, animals remained motionless but with wide open eyes, fully raised ears and no miosis. In turn, substance P caused restlessness and increased locomotion. These results suggest that linear peptides may play a role in the functioning of the central nervous system. 37 references. (Author abstract modified)

215696 Siegel, R. K.; Gusewelle, B. E.; Jarvik, M. E. Department of Pharmacology, University of California, Los Angeles, CA 90024 **Naloxone-induced jumping in morphine dependent mice: stimulous control and motivation.** International Pharmacopsychiatry (Basel). 10(1):17-23, 1975.

Stimulus control and motivation in naloxone induced jumping in morphine dependent mice were studied. At 2 in, which permitted tactile contact with the cover, no jumps occurred in the light or the dark; at 5-11 in, a high inncidence of jumping occurred in both the light and the dark; at 23 in, too high for the animal to reach, relatively few jumps occurred in the light but many occurred in the dark. In another study, similar groups were singly tested in the light after naloxone on each of five circular platforms (18 in high, 3-48 in diameter). As the diameter increased, the number of mice jumping to the floor showed a linear decrease concomitant with an increase in latency. This suggests that jumping is controlled by visual and tactile cues; mice do not jump when escape is prevented by a cover which can be touched or a height which cannot be reached; but do jump when such cues are eliminated by intermediate heights or darkness. Latency varies with size of immediate explorable environment. 18 references. (Author abstract modified)

215704 Smith, Gerard P.; Levin, Barry E.; Ervin, Gregory N. E. W. Bourne Laboratory, New York Hospital, Westchester Division, White Plains, NY 10605 **Loss of active avoidance responding after lateral hypothalamic injections of 6-hydroxydopamine.** Brain Research (Amsterdam). 88(3):483-498, 1975.

The effects of 6-hydroxydopamine (6-OHDA) along the medial forebrain bundle in the lateral hypothalamus of rats were studied. Ss failed to acquire a one way active avoidance response or failed to perform a previously acquired active avoidance response. Such rats, however, acquired a passive avoidance response and a conditioned taste aversion normally. Thus the effect of lateral hypothalamic injections of 6-OHDA was not a total loss of the capacity to acquire or perform conditioned responses, but was a failure to initiate forward movement in the presence of a conditional stimulus. Failure to acquire or perform the active avoidance responses was correlated with the loss of hypothalamic, striatal and forebrain catecholamines produced by lateral hypothalamic 6-OHDA injections. It is concluded that medial 6-OHDA injections did not damage the same catecholaminergic terminal fields as lateral 6-OHDA injections and that the integrity of the terminal fields damaged by lateral 6-OHDA injections is necessary for active avoidance responding. 49 references. (Author abstract modified)

215722 McMillan, D. E.; Leander, J. D. Department of Pharmacology, School of Medicine, University of North Carolina, Chapel Hill, NC 27514 **Drugs and punished responding. V. Effects of drugs on responding suppressed by response-dependent and response-independent electric shock.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 213(1):22-27, 1975.

In a study of drugs and punished responding, a procedure was used where responses by a pigeon produced electric shock both to that pigeon (response dependent shock) and to another pigeon (response independent shock) working under the same schedule of food presentation. Both response dependent and response independent shock partially suppressed responding. Pentobarbital, chlordiazepoxide and ethanol increased responding suppressed by response dependent shock, but only pentobarbital increased responding suppressed by response independent shock. Morphine, d-amphetamine, chlorpromazine, doxepin, and pentazocine either had no effect, or further decreased rates of responding suppressed by response dependent or response independent shock. 18 references. (Author abstract)

215732 Poschel, B. P. H.; Ninteman, F. W.; McLean, J. R.; Potoczak, D. Department of Pharmacology, Parke, Davis and Company, Research and Development Division, Ann Arbor, MI 48106 **Intracranial reward after 5,6-dihydroxytryptamine: further evidence for serotonin's inhibitory role.** Life Sciences 15(8):1515-1522, 1974.

In a study of serotonin's inhibitory role, 1 intraventricular injection of 5,6-dihydroxytryptamine produced, 24 hr later, a marked increase in rates of medial forebrain bundle self-stimulation. Whole brain serotonin levels were selectively depressed at this time, presumably because of the destructive effect on serotonin containing neuron terminals. When whole brain serotonin levels had recovered fairly close to normal, the excitatory effect had disappeared. In rats having self-stimulation electrodes positioned at slight distances from the medial forebrain bundle, the excitatory effect never appeared. These results support the theory that serotonergic neurons in the medial forebrain bundle are part of an inhibitory system subserving reward and motivational mechanisms. The results show the great importance of electrode placement as a determinant of a drug's effect on self-stimulation. 13 references. (Author abstract)

215749 Wisniewski, Konstanty; Bodzenta, Anna. Department of Pharmacology, School of Medicine in Bialystok, Mickiewicza 2, 15-222 Bialystok, Poland **Kinins and central effects of the acetylcholine.** Acta Neurobiologiae Experimentalis (Warszawa). 35(1):85-92, 1975.

The interaction between kinins formed in central nervous system and acetylcholine (ACh) was studied. Endogenous ACh in excess acted psychodepressively on the animal's behavior as evaluated with Lat's test. This effect was more intense in those rats in which the activity of kinin forming enzymes in the nervous tissue had been increased with either kallikrein or bradykinin. Both kallikrein and bradykinin intensified the psychodepressive action of exogenous ACh given into the brain ventricle. Results show that kinins can enhance the inhibitory central action of ACh. 18 references. (Author abstract)

215789 Burov, Yu. V.; Speranskaya, N. P. Laboratoriya farmakoterapii ekstremal'nykh sostoyaniy, Instituta farmakologii AMN SSSR, Moscow **/An analysis of neurochemical mechanisms of one form of intraspecies behavior./** Analiz neyrokhimicheskikh mekhanizmov odnoy iz form vnutrividovogo povedeniya. Zhurnal vysshey nervnoy deyatel'nosti imeni I. P. Pavlova (Moskva). 24(2):301-305, 1974.

The influence of neurochemical mechanisms in the formation and realization of an avoidance reaction to painful electrical stimulation was investigated pharmacologically in rats. Injections of the muscarinic cholinolytics amizyl and atropine, or alpha-adrenoblocker phentolamine, in doses which displayed their central effects, were found to depress avoidance reaction in one rat to pain stimulation of another. The nicotinic cholinolytic aprophene, beta-adrenoblocker dicholorisoproterenol, antagonists of serotonin, morphine and LSD, in doses eliciting corresponding central effects, did not influence the avoidance reaction. Muscarinic cholinomimetic arecoline and adrenomimetic amphetamine accelerated the avoidance reaction. The central muscarinic cholinergic and

alpha-adrenergic structures were tentatively concluded to be involved in the formation and elaboration of the avoidance reaction of one rat to the stimulation of another. 19 references. (Journal abstract modified)

215798 Ropert, R. 5, avenue Daniel-Lesueur, Paris 7e **/The use of cyamepromazine in small doses in treatment of nonpsychotic disturbances./** L'emploi de la cyamepromazine a faible dose dans le traitement des affections non psychotiques. Information Psychiatrique (Paris). 51(1):87-94, 1975.

Cyamepromazine in 100mg doses was used for treatment of nonpsychotic disturbances. Dosage used varied from 50 to 100mg daily in 74% of the 129 cases treated; the average duration of treatment was 63 days. Cyamepromazine had an anxiolytic action which is useful not only in treating psychotic disturbances and their sequelae, but also in treating character disorders and neuroses. It also has a sedative effect, which makes possible the treatment of different types of neuroses, neurotic and reactive depressive syndromes, and certain types of insomnia. With doses of 50-75mg per day, no annoying side-effects were noted. The use of a 25mg dose permitted considerable reduction of emergent vigilance and asthenic reactions. 16 references. (Author abstract modified)

215968 Downs, David A.; Woods, James H. Department of Pharmacology, University of Michigan Medical School, M6322 Medical Science I, Ann Arbor, MI 48104 **Fixed-ratio escape and avoidance-escape from naloxone in morphine-dependent monkeys: effects of naloxone dose and morphine pretreatment.** Journal of Experimental Analysis of behavior. 23(3):415-427, 1975.

The effects of dose on responding under fixed-ratio schedules of escape and avoidance - escape from naloxone in morphine dependent rhesus monkeys were examined. Lever pressing was maintained by morphine injections during four equally spaced sessions each day. During other periods, lever pressing was maintained by timeout from a continuous naloxone infusion or from a stimulus that preceded naloxone injections, or termination of the injections. As naloxone dose increased in the escape procedure, response rate increased to a maximum and then decreased. In the avoidance - escape procedure, response rate generally increased as naloxone dose increased, but the changes in rate were small compared to the escape procedure. Substitution of saline for naloxone in the escape procedure led to very low response rates. In the avoidance - escape procedure, rate decrements produced by saline substitution were related to the behavioral history of the monkey. Morphine pretreatment produced dose dependent decreases in response rates in both procedures. The rate decreasing effects of morphine were exacerbated when no naloxone was delivered in the escape procedure. 26 references. (Author abstract modified)

215969 Thompson, Donald M. Department of Pharmacology, Georgetown University Schools of Medicine and Dentistry, 3900 Reservoir Rd., N.W., Washington, DC 20007 **Repeated acquisition of response sequences: stimulus control and drugs.** Journal of Experimental Analysis of Behavior. 23(3):429-436, 1975.

The similarity between the repeated acquisition of tandem response sequences and chain sequences under phenobarbital and chlordiazepoxide administration was determined in pigeons. Pigeons obtained food by making four responses on three keys in a specified sequence. Under the tandem learning condition, all three keys were the same color throughout the response sequence, and the sequence was changed from session to session. After total errors per session and within session error reduction had stabilized, the effects of varying doses of phenobarbital and chlordiazepoxide were assessed. Drug tests were also conducted under a tandem performance condition in which the response sequence was the same from session to session. As in chain conditions, the largest dose of each drug impaired overall accuracy. Under chain and tandem learning, the error rate decreased within each session, but the degree of negative acceleration was less in the drug sessions than in the control sessions. In chain and tandem performance conditions, the error rate was relatively constant across trials, but was higher in the drug sessions than in the control sessions. Chain learning proved most sensitive to drugs. 16 references. (Author abstract modified)

216494 Ely, Daniel L.; Henry, James P.; Jarosz, Christopher J. Department of Biology, University of California, Riverside, CA 92502 **Effects of marihuana (delta9-THC) on behavior patterns and social roles in colonies of CBA mice.** Behavioral Biology. 13(3):263-276, 1975.

The effects of marihuana (delta9-THC) upon dominant and subordinate male behavior profiles were continuously observed in mice socially interacting in population cages. Ethologically oriented observations consisting of entry - exit rates, patterns of spontaneous behavior, and elapsed time in each functional area were made. The subordinates showed no significant change in their pattern of low locomotor activity after a single intravenous dose. By contrast, the high activity dominants showed a significant reduction in entry - exit rates and in their patrol patterns. A dose of 0.5mg/kg delta9-THC significantly decreased the dominant male's aggressive response to an intruder, but did not alter his social status. It is concluded that the behavioral effect of delta9-THC in a freely interacting, mixed sex group of rodents living in population cages is dependent upon social position in the hierarchy and upon the social composition of the group. 25 references. (Author abstract modified)

217064 Ostrovskaya, R. U.; Molodavkin, G. M.; Porfir'yeva, R. P.; Zubovskaya, A. M. Institut farmakologii AMN SSSR, Moscow **/The mechanism of anticonvulsive action of diazepam./** K mekhanizmu protivosudorozhnogo deystviya diazepama. Byulleten' eksperimental'noy biologii i meditsiny (Moskva). 79(3):50-53, 1975.

The effectiveness of diazepam in preventing convulsive seizures was investigated in mice. Mice were subjected to injections of thiosemicarbazide, and diazepam was injected 15 minutes later. Diazepam was found to induce a decrease in the intracortical response of the motor cortex during the recovery cycles, thereby inhancing cerebral inhibitory processes. An antagonistic relationship was observed between diazepam and thiosemicarbazide. Diazepam was capable of increasing gamma-aminobutyric acid (GABA) content in the brain by suppressing GABA transaminase activity in the mitochondrial fraction of the brain tissue. Diazepam was concluded to be highly effective in preventing convulsive seizures associated with GABA insufficiency. 11 references. (Journal abstract modified)

217152 Creese, Ian. Johns Hopkins University School of Medicine, 725 N. Wolfe St., Baltimore, MD 21205 **Behavioural evidence of dopamine receptor stimulation by piribedil (ET495) and its metabolite S584.** European Journal of Pharmacology (Amsterdam). 28(1):55-58, 1974.

Behavioral evidence of dopamine receptor stimulation by piribedil (ET495) and its metabolite S584 is presented. Piribedil

(ET495) and its catechol metabolite S584 induced enhanced stereotyped behavior and locomotor activity in adult rats treated as neonates with intraventricular 6-hydroxydopamine. These same rats also showed an enhanced behavioral response to apomorphine, a directly acting dopamine agonist, but a blocked behavioral response to amphetamine, an indirectly acting dopamine agonist. This suggests that the dopaminergic action of piribedil is postsynaptic in origin and may be mediated via its active metabolite S584. 15 references. (Author abstract)

217218 Breese, George R.; Cooper, Barrett R.; Hollister, Alan S. Department of Pharmacology, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Relationship of biogenic amines to behavior.** Journal of Psychiatric Research (Oxford). 11:125-133, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, data concerned with the biochemical basis of the behavioral effects of amphetamine and the neural systems responsible for the maintenance of self-stimulation was discussed. Dopaminergic fibers seem to play an important role in the maintenance of intracranial self-stimulation. Amphetamine induced motor activity as well as the stereotypies produced by this drug were also found to be dependent upon intact dopaminergic fibers. Evidence was presented that serotonin fibers may modulate the behavioral actions of amphetamine by acting as an inhibitory transmitter. 54 references. (Author abstract modified)

217440 Lycke, E.; Roos, B.-E. Department of Virology and Pharmacology, University of Goteborg, Goteborg, Sweden **Influence of changes in brain monoamine metabolism on behaviour of herpes simplex-infected mice.** Journal of the Neurological Sciences (Amsterdam). 22(3):277-289, 1974.

In herpes simplex virus (HSV) infected mice hypermotility was observed associated with an increased release of transmitter from adrenergic neurons. Inhibition of dopamine (DA) metabolism by the administration of alpha-methyltrosine to the infected mice decreased motility rate counts, while p-chlorophenylalanine, by inhibiting the formation of 5-hydroxytryptamine (5-HT) caused an increase in rate of motility. Pimozide and phenoxybenzamine, used for blocking DA and noradrenaline (NA) receptors, respectively, were both observed to reduce the hypermotility efficiently. Administration of FLA-63 as an inhibitor of NA metabolism was associated with increased death rates in HSV infected mice. Changes in behavior towards aggression were encountered when levodopa was administered to HSV infected mice and when apomorphine and clonidine were used for stimulation of the receptor functions of adrenergic neurons. The observations reported suggest that hypermotility, excitation and aggression might all be symptoms associated with a pathologicaly increased activity of adrenergic neurons. 21 references. (Author abstract)

217451 Fog, Rasmus. Psychopharmacological Laboratory, Department E, St. Hans Hospital, DK-4000 Roskilde, Denmark **Neuroleptic action of clozapine injected into various brain areas in rats.** International Pharmacopsychiatry (Basel). 10(2):89-93, 1975.

Neuroleptic action of clozapine injected into various brain areas were examined in rats. Bilateral microinjections of clozapine into the corpus striatum of rats antagonized amphetamine induced stereotypy and caused catalepsy. These two neuroleptic effects are not seen after subcutaneous or oral administration of clozapine. The effects were a little weaker than those seen after chlorpromazine. No neuroleptic effects were observed, when placebo was injected intrastriatally, nor when clozapine was injected into the hippocampus or the thalamus. 14 references. (Author abstract)

217458 Leander, J. David. Dept. of Pharmacology, School of Medicine, Swing Bldg., University of North Carolina, Chapel Hill, NC 27514 **Rate-dependent effects of drugs. II. Effects of some major tranquilizers on multiple fixed-ratio, fixed-interval schedule performance.** Journal of Pharmacology and Experimental Therapeutics. 193(2):689-700, 1975.

The effects of promazine, chlorpromazine, triflupromazine, prochlorperazine, trifluoperazine, perphenazine, fluphenazine, haloperidol, benzquinamide, tetrabenazine and chlorprothixene were determined on the rate of conditioned keypecking of pigeons under a multiple fixed-ratio 30, fixed-interval 5 minute schedule of food presentation. Chlorpromazine, prochlorperazine, perphenazine, chlorprothixene and tetrabenazine decreased responding relatively more within the fixed-interval component than within the fixed-ratio component and also produced rate dependent effects within the fixed interval component, increasing the low rates of responding early in the fixed-interval but decreasing the high rates of responding in the terminal parts of the fixed interval. Triflupromazine, trifluoperazine, fluphenazine and haloperidol also decreased responding relatively more within the fixed-interval component than within the fixed-ratio component, but did not produce rate dependent effects within the fixed-interval component. There was a structure - activity relationship between the chemical group on the benzene ring of the phenothiazine nucleus and the rate dependent effect on responding within the fixed-interval component. (Author abstract modified)

217459 Brown, Roger M.; Seiden, Lewis S. NIH, Bethesda, MD 20014 **Interresponse time changes as a function of water deprivation and amphetamine.** Journal of Pharmacology and Experimental Therapeutics. 193(2):701-712, 1975.

Changes in interresponse time (IRT) induced by doses of amphetamine or alterations in level of water deprivation in the rat were compared and contrasted. Short IRTs that characterized fixed-ratio 20 performance were resistant to change with increasing doses of amphetamine, but were increased in duration with decreasing water deprivation. Animals responding on a fixed-interval 90 second schedule showed a decreased postreinforcement pause after amphetamine, but an increased postreinforcement pause after access to water. The combined effects of pression water consumption and d-amphetamine administration on variable interval performances was also examined. Making water available before the session lowered the amphetamine dose - response curve along the vertical axis, suggesting that amphetamine did not mimic satiation. In most cases the effect of amphetamine and changing levels of water deprivation were dissimilar in their effects on IRT distributions, suggesting that amphetamine does not exert its major action on behavior through its adipsic effect. (Author abstract modified)

217461 Pijnenburg, A. J. J.; Honig, W. M. M.; Van Rossum, J. M. Department of Pharmacology, University of Nijmegen, Geert Grooteplein Noord 21, Nijmegen, The Netherlands **Inhibition of d-amphetamine-induced locomotor activity by injection of haloperidol into the nucleus accumbens of the rat.** Psychopharmacologia (Berlin). 41(2):87-95, 1975.

The effect of intracerebral administration of antagonists of dopamine and noradrenaline upon the locomotor stimulation induced by intraperitoneal injection of d-amphetamine sulfate

in rats was investigated. Injection of low doses of the dopamine antagonist haloperidol bilaterally into the nucleus accumbens antagonized the locomotor stimulation following d-amphetamine. No significant inhibition was observed following administration of the alpha-adrenergic antagonist phentolamine or the beta-adrenergic antagonist propranolol into the nucleus accumbens. Injection of the same doses of haloperidol into the caudate nucleus did not inhibit the d-amphetamine induced locomotor activity, in contrast to the effects seen following injection into the nucleus accumbens. The results confirm the significance of dopaminergic mechanisms for the locomotor stimulant effect of d-amphetamine and indicate that the mesolimbic dopamine system plays an important role in this respect. 50 references. (Author abstract)

217463 Leathwood, P. D.; Bush, M. S.; Mauron, J. Research Department, Nestle Products Technical Assistance Co. Ltd., CH-1800 Vevey, Switzerland **The effects of chlordiazepoxide on avoidance performance of mice subjected to undernutrition or handling stress in early life.** Psychopharmacologia (Berlin). 41(2):105-109, 1975.

The effects of early undernutrition by rearing in large litters and an early handling stress, on avoidance learning in Swiss white mice were examined. The two treatments, the first leading to permanent physical stunting and the second not, had similar and additive detrimental effects on avoidance performance. Treatment with the minor tranquillizer Chlordiazepoxide improved performance in all groups but had a proportionately greater effect on previously undernourished, handled mice. Thus the poor avoidance performance of mice reared in large litters appears to be largely independent of the growth stunting effect and more closely related to an elevated stress response produced by stress in early life. 16 references. (Author abstract)

217464 Van Abeelen, J. H. F.; Ellenbroek, G. A.; Wigman, H. G. A. J. Genetics Laboratory, University of Nijmegen, The Netherlands **Exploratory behaviour in two selectively-bred lines of mice after intrahippocampal injection of methylscopolamine.** Psychopharmacologia (Berlin). 41(2):111-112, 1975.

The temporal course of exploratory behavior in male mice from two selected lines SRH (showing frequent rearing responses) and SRL (with less frequent rearing), following injection of methylscopolamine into the hippocampus was studied. The anticholinergic drug decreased exploration in the SRH line and prolonged it in the SRL line. The experiment supplies further proof that a cholinergic system in this brain area regulates response to novelty and that this system is controlled by genetic factors. 8 references. (Author abstract)

217465 Banerjee, Utpal. Department of Pharmacology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia **Conditioned learning in young rats born of drug-addicted parents and raised on addictive drugs.** Psychopharmacologia (Berlin). 41(2):113-116, 1975.

In a study of conditioned learning in young rats, ratlings born of six drug addicted and a control group of parents rats were raised under the influence of the same drugs administered in drinking water. They were trained in a conditioned avoidance paradigm (CAR) from the 7th week when the drugs were withdrawn except in two subgroups of flurazepam and morphine. The growth rate was not appreciably impaired except for temporary slowness in morphine and alcohol raised rats; it was faster in phenobarbitone and meprobamate raised rats. The CAR acquisition rates of the treatment groups were quite close and parallel to that of the controls except for the morphine, meprobamate, medazepam and the two drug trained subgroups; whereas, the rats raised on low dose morphine showed a faster than control acquisition rate. No evidence of state dependent learning was obtained. 9 references. (Author abstract)

217466 Sansone, Mario. Laboratoria di Psicobiologia e Psicofarmacologia, C.N.R., Via Reno, 1, I00198 Rome **Facilitation of avoidance learning by chlordiazepoxide-amphetamine combinations in mice.** Psychopharmacologia (Berlin). 41(2):117-121, 1975.

Chlordiazepoxide and amphetamine, given separately or in combination, were tested in mice subjected to 5 100 trial avoidance sessions in the shuttle box. Facilitation of avoidance responding was much more evident and statistically significant when the two drugs were combined. Drug mixtures produced effects which could not be obtained when the drugs were given separately. 24 references. (Author abstract)

217468 Graeff, F. G.; De Oliveira, L. Departmento de Farmacologia, Faculdade de Medicina, 14 100 Ribeirao Preto, Sao Paulo, Brasil **Influence of response topography on the effect of apomorphine and amphetamine on operant behavior of pigeons.** Psychopharmacologia (Berlin). 41(2):127-132, 1975.

The influence of response topography on the effect of apomorphine and amphetamine on operant behavior of pigeons was examined. Effective doses of apomorphine caused dose dependent decreases on treadle pressing rates in all animals. Similarly, key pecking rates were decreased by increasing doses of apomorphine in two of the five pigeons. However, dose dependent increases in key pecking rates were caused by apomorphine in the other three birds. Observation of the animals under the effect of apomorphine showed continuous pecking at the operative key in these three animals while the other two pecked at different places of the floor and walls of the experimental chamber. Appropriate doses of amphetamine caused rate-increasing effects on key pecking as well as treadle pressing rates of all pigeons. These results suggest that the increases in key pecking rate caused by apomorphine in some pigeons in a conventional operant situation are due to the orientation of the drug induced stereotyped pecking toward the response key, as a consequence of the topographic compatibility between this behavioral effect of apomorphine and the operant selected for study. 36 references. (Author abstract modified)

217470 Connelly, John F.; Connelly, Jacqueline M.; Phifer, Ronald. Department of Psychology, Kansas State College, Pittsburg, KS 66762 **Disruption of state-dependent learning (memory retrieval) by emotionally-important stimuli.** Psychopharmacologia (Berlin). 41(2):139-143, 1975.

In a study of state dependent learning (SOL), groups were trained each day in one drug state (either Librium, 40mg/kg or sterile water) and then given nonshock test trials in both drug states. SDL Ss showed drug dependent retention since they turned randomly in opposite state test trials and significantly above random level when in the training drug state. For the transfer Ss, a 1 kHz tone was simultaneously paired with foot shock in training, and continued to be sounded on every nonshock test trial. Transfer Ss turned in the training direction regardless of drug state. Drug-dependence in the SDL groups and transfer in the transfer groups were also demonstrated in response latencies. The tones were emotional memory prompters initiating some process that mediated transfer between drug states. The theoretical importance of these results were discussed in relation to energizing and directing functions of

emotions and symmetrical and asymmetrical transfer. 13 references. (Author abstract modified)

217474 Ten Ham, M.; De Jong, Y. National Institute of Public Health, Laboratory of Pharmacology, P.O. Box 1, Bilthoven, The Netherlands **Absence of interaction between delta9-tetrahydrocannabinol (delta9-THC) and cannabidiol (CBD) in aggression, muscle control and body temperature experiments in mice.** Psychopharmacologia (Berlin). 41(2):169-174, 1975.

The effects of the hashish constituents delta9-tetrahydrocannabinol (THC) and cannabidiol (CBD) on mice were examined. THC produced a dose dependent depression of aggression in isolated mice and a dose dependent depression of body temperature in group caged mice. The drug did not alter motor coordination. CBD showed a small, nonsignificant influence on aggressiveness, and no influence on body temperature and muscle control. The same experiments were carried out with combinations of THC and CBD in several dosages. No interaction between the two compound was seen. This means that there can only be an additive action and not potentiation in the pharmacological sense. It also means that the in vitro inhibition by CBD of the drug metabolizing enzymes, responsible for biotransformation of THC, is not strong enough to result in changed effects of THC in the living animal. 19 references. (Author abstract)

217475 Pijnenburg, A. J. J.; Honig, W. M. M.; Van Rossum, J. M. Department of Pharmacology, University of Nijmegen, Geert Grooteplein Noord 21, Nijmegen, The Netherlands **Effects of antagonists upon locomotor stimulation induced by injection of dopamine and noradrenaline into the nucleus accumbens of nialamide-pretreated rats.** Psychopharmacologia (Berlin). 41(2):175-180, 1975.

The effects of injections of monoamines, alone and in combination with different antagonists, bilaterally into the nucleus accumbens of nialamide pretreated rats were investigated. Dopamine was found to produce a stronger stimulation of locomotr activity than noradrenaline, whereas serotonin was effective only in a small number of animals, in which the duration of locomotr stimulation was shorter than after dopamine or noradrenaline. The effects of both dopamine and noradrenaline were completely antagnoized by administration of a small dose of the dopamine antagonist haloperidol, administered bilaterally 15 min after the catecholamines. The alpha-adrenergic antagonist phentolamine did not inhibit the effect of noradrenaline but, on the contrary, potentiated and considerably prolonged the duration of locomotor stimulation. Also, the effect of dopamine was potentiated and prolonged by phentolamine. Bilateral injection of phentolamine alone had no influence upon locomotor activity. The effect of noradrenaline was not clearly inhibited nor potentiated by the beta-adrenergic antagonist propranolol. It is suggested that the stimulation of locomotor activity induced by injection of noradrenaline into the nucleus accumbens of bialamide pretreated rats is brought about via dopaminergic mechanisms. 24 references. (Author abstract)

217519 Luthra, Yugal K.; Rosenkrantz, Harris; Heyman, Irwin A.; Braude, Monique C. Mason Research Institute, Worcester, MA 01608 **Differential neurochemistry and temporal pattern in rats treated orally with delta9-tetrahydrocannabinol for periods up to six months.** Toxicology and Applied Pharmacology. 32(2):418-431, 1975.

Differential neurochemistry and temporal patterns were examined in rats treated orally with delta9-tetrahydrocannabinol for periods up to 6 months. Groups of male and female Fischer rats were treated orally with THC doses of 2, 10, or 50mg/kg for 28, 90, 180 days. Another group of rats treated for 180 days was studied after a 30 day recovery period. The lowest dose employed in the present study corresponded to THC content of one high-grade marihuana cigarette and the intermediate dose simulated the THC content of one hashish cigarette. In the first 10 days central nervous system (CNS) depression, incoordination, ataxia and passivity, poikilothermia, and hypopnea occurred to which tolerance developed. During days 10-20, irritability, hypersensitivity, hyperactivity, and aggression predominated. Peaks of fighting occurred between days 20-100 among 60% of the animals at higher doses. Tremors and clonic convulsions appeared after day 70 in 50% of the animals at 50mg/kg and 12% at 10mg/kg. Tolerance developed to CNS stimulation, fighting, and neurotoxicity. 41 references. (Author abstract modified)

217521 Sabelli, H. C.; Vazquez, A. J.; Flavin, D. Department of Pharmacology, University of Health Sciences, Chicago Medical School, 2020 West Ogden Avenue, Chicago, IL 60612 **Behavioral and electrophysiological effects of phenylethanolamine and 2-phenylethylamine.** Psychopharmacologia (Berlin). 42(2):117-125, 1975.

The electrophysiological and behavioral effects of phenylethanolamine (OHPEA) and of its precursor 2-phenylethylamine (PEA) were studied in mice and rabbits. In animals pretreated with monoamine oxidase inhibitors (MAOI), PEA was found to exert strong amphetamine-like effects, electroencephalogram alerting, reduction of visual evoked responses, increased locomotor activity, and blockade of tonic seizures induced by electroshock. OHPEA exerted weaker amphetamine like effects. Inhibition of dopamine-beta-hydroxylase increased most of the effects of PEA. In nonpretreated animals, OHPEA was found to shorten electroshock latency and to prolong the duration of visual evoked responses. PEA (but not OHPEA) potentiated the excitement induced by delta9-tetrahydrocannabinol in MAOI pretreated mice. Reserpine pretreatment reduced but did not abolish the central nervous system effects of OHPEA and PEA. One may speculate that endogenous PEA is more likely to serve as a modulator for ergotropic functions than is endogenous OHPEA. 23 references. (Author abstract)

217524 Figler, Michael H.; Klein, Richard M.; Thompson, Christine S. Department of Psychology, Towson State College, Baltimore, MD 21204 **Chlordiazepoxide (Librium)-induced changes in intraspecific attack and selected non-agonistic behaviors in male Siamese fighting fish.** Psychopharmacologia (Berlin). 42(2):139-145, 1975.

The effects of chlordiazepoxide on intraspecific attack behavior and selected nonaggressive behaviors in male Siamese fighting fish were examined. In Exp. 1, pairs of fish fought while immersed in chlordiazepoxide, or plain water. The drug groups showed significantly less attack (e.g.,biting, jawlocking) than the control group, without noticeable behavioral toxicity. Also, in the drug groups alone, some variants of the copulatory clasp, seen in normal mating, occurred in many pairs. In Exp. 2, individual fish were isolated in one of the same doses or plain water for a period equivalent to that of Exp. 1. These doses produced no changes in measures of arousal, locomotion, and feeding behavior, as compared to the control condition. The drug related appearance of the internale mating like behavior is discussed in terms of a theoretical formulation postulating a mutually inhibitory relationship between sex and aggression in fish. 21 references. (Author abstract)

217525 Fleming, Jan C.; Broadhurst, P. L. P. O. Box 174, Dickson, ACT 2602, Australia **The effects of nicotine on two-way avoidance conditioning in bi-directionally selected strains of rats.** Psychopharmacologia (Berlin). 42(2):147-152, 1975.

The effects of nicotine on two-way avoidance conditioning in bidirectionally selected strains of rats were examined. Rats of both sexes from the genetically selected Roman High Avoidance (RHA), the Roman Low Avoidance (RLA) and the Roman Control (RCA) strains were given one 30 min session of two-way escape - avoidance conditioning (30 trials) in a shuttlebox with a buzzar as the conditioned stimulus and shock as the unconditioned stimulus in a factorial design involving three time intervals following one subcutaneous injection of saline or of nicotine in five doses. While the number of avoidance responses showed the expected strain differences, no effect of dose or delay interval could be detected. Avoidance and escape latencies and intertrial activity showed some effects of these variables, especially in interaction with sex and strain. Dose determined presessional activity, but its effect was strain dependent. The failure to confirm previous findings is discussed in the context of other instances in the literature, and the results of an operant experiment confirming the continuing sensitivity of the Roman strains to the effects of nicotine are reported. 42 references. (Author abstract)

217526 Katz, R. J.; Thomas, E. Department of Psychology, Bryn Mawr College, Bryn Mawr, PA 19010 **Effects of scopolamine and alpha-methylparatyrosine upon predatory attack in cats.** Psychopharmacologia (Berlin). 42(2):153-157, 1975.

The effects of scopolamine were compared with the effects of alpha-methylparatyrosine methyl ester (AMPT) upon several aspects of electrically elicited predatory attack in cats. Thresholds of current necessary to elicit predation increased under both drugs. Specific deficits developed in suprathreshold predatory patterns for both drugs compared with nondrug baselines. Scopolamine suppressed all aspects of attack, while AMPT suppressed approach of the attack object while leaving reflexive biting intact. 18 references. (Author abstract)

217530 Broekkamp, C. L. E.; Pijnenburg, A. J. J.; Cools, A. R.; Van Rossum, J. M. Department of Pharmacology, Univerisity of Nijmegen, Geert Grooteplein Noord 21, Nijmegen, The Netherlands **The effect of microinjections of amphetamine into the neostriatum and the nucleus accumbens on self-stimulation behaviour.** Psychopharmacologia (Berlin). 42(2):179-183, 1975.

The effect of microinjections of dexamphetamine chloride into the neostriatum, the nucleus accumbens, the anterior hypothalamus, and the ventricular system on self-stimulation with electrodes in the ventral tegmentum was studied. Unilateral injections into the anterior hypothalamus produced no effect. Injections into the neostriatum tended to depress the self-stimulation rate, whereas injections into the nucleus accumbens increased the rate markedly. Bilateral injections into the nucleus accumbens were more effective than unilateral injections and were as effective as systemic injections of 1mg/kg amphetamine. Bilateral injections into the neostriatum also increased the self-stimulation rate. Injections into the ventricular system resulted in a smaller increase which was not statistically significant. These results are discussed in relation to the involvement of the dopaminergic system in the maintenance of self-stimulation behaviour. 24 references. (Author abstract)

217531 Schechter, Martin D.; Cook, Peter G. Department of Pharmacology, Eastern Virginia School, Norfolk, VA 23507 **Dopaminergic mediation of the interoceptive cue produced by d-amphetamine in rats.** Psychopharmacologia (Berlin). 42(2):185-193, 1975.

Brain biogenic amine depletors and selective receptor antagonists were employed to observe their effect on the ability of rats to discriminate amphetamine in a shock - escape apparatus. After rats were trained to differentiate between the effects of d-amphetamine and saline in a state dependent task, pretreatment with the tyrosine hydroxylase inhibitor, alpha-methyl-p-tyrosine, significantly decreased amphetamine discrimination. Pretreatment with the dopamine-beta-hydroxylase inhibitor, disulfiram, or with the tryptophan hydroxylase inhibitor, p-chloro-phenylalanine, was observed to have no effect on the rats' ability to discriminate d-amphetamine. Administration of haloperidol, a selective dopamine receptor blocker, completely abolished the amphetamine discrimination, whereas alpha-adrenergic and beta-adrenergic receptor blockade had no effect. Apomorphine, a dopamine receptor stimulant, produced amphetamine-like responses and this was, likewise, abolished by pretreatment with haloperidol. These data suggest that dopaminergic systems mediate the interoceptive cue produced by d-amphetamine in rats, and these results are discussed in relation to possible dopamine mediation of amphetamine psychosis and paranoid schizophrenia. 48 references. (Author abstract)

217532 Palermo Neto, J.; Nunes, J. F.; Carvalho, F. V. Faculdade de Medicina, Veterinaria, Universidade de Sao Paulo, Cidade Universitaria A.S.O., Sad Paulo, Brazil **The effects of chronic cannabis treatment upon brain 5-hydroxytryptamine, plasma corticosterone and aggressive behavior in female rats with different hormonal status.** Psychopharmacologia (Berlin). 42(2):195-200, 1975.

In a study of the effects of chronic cannabis treatment, ovariectomized rats, chronically treated with cannabis extract or control solution, were given different hormonal treatments. Results indicated that both cannabis treated and estrogen treated animals were more aggressive than controls. Aggressiveness was virtually abolished when cannabis treated females were made sexually receptive by estrogen and progesterone treatments. After 25 days of cannabis or control solution treatment, all subjects were sacrificed. The levels and turnover rate of brain 5-hydroxytryptamine (5-HT) and peripheral plasma corticosterone were then assayed. Data indicated both a significant inverse relationship between plasma corticosterone and whole brain levels of 5-HT for all groups and a significant positive relationship between aggressive behavior and plasma corticosterone in all groups that were fighting prior to decapitation. Results are tentatively explained, suggesting that the variability of the female response to stress during the different phases of the estrus cycle, permitted them to perform differently after chronic cannabis treatment. 5-HT is apparently involved, either directly in its effects on aggressive behavior or indirectly through the pituitary - adrenocortical axis activation. 33 references. (Author abstract)

217533 Gaillard, Anthony W. K.; Sanders, Andries F. Institute for Perception TNO, Soesterberg, The Netherlands **Some effects of ACTH 4-10 on performance during a serial reaction task.** Psychopharmacologia (Berlin). 42(2):201-208, 1975.

The effects of ACTH4-10 on performance during a serial reation reaction task were examined. The subjects injected with ACTH4-10 showed a larger improvement in reaction time during the experimental session than the placebo group. This effect disappeared in a short retest, which was given half an hour after the experimental session. These results suggest that ACTH 4-10 has no effect on skill acquisition, but counteracts

the buildup of reactive inhibition during the experimental session; that is, the peptide suppresses the decrease in motivation, which usually occurs during continuous performance tasks. This notion is confirmed by an analysis of the frequency distributions of the reaction times. Treatment effects were only found for the long reaction times. Long reaction times tend to occur with increasing frequency as a function of time on task and are an indication for the level of motivation of the subject. It was concluded that ACTH4-10 counteracts the usual decay in performance as a function of time on task due to increasing boredom and mental fatigue. 15 references. (Author abstract modified)

217541 Jones, B. E.; Prada, J. A. NIDA Addiction Research Center, P.O. Box 12390, Lexington, KY 40511 **Drug-seeking behavior during methadone maintenance.** Psychopharmacologia (Berlin). 41(1):7-10, 1975.

In a study of drug seeking behavior during methadone maintenance, six subjects were given the opportunity to work for saline placebo and hydromorphone (4mg i.v.)several times weekly before and during a period of maintenance on methadone (100mg p.o. daily). Measures of pupillary change and reports of liking in response to hydromorphone dropped to saline control levels when the daily dose of methadone was approximately 60mg. Half of the subjects continued to work intermittently for hydromorphone for 4 weeks while they were receiving 100mg of methadone daily. These data support the assumption that methadone maintenance reduces the reinforcement value of other opiates and behaviors associated with obtaining them. 4 references. (Author abstract)

217542 McKearney James W.; Barrett, James E. Worcester Foundation for Experimental Biology, Shrewsbury, MA 01545 **Punished behavior: increases in responding after d-amphetamine.** Psychopharmacologia (Berlin). 41(1):23-26, 1975.

The effects of d-amphetamine on punished responding were examined. Responding maintained in squirrel monkeys under a 10 min fixed-interval schedule of food presentation was suppressed by presenting a shock every 30th response (punishment). During alternate 10 min periods of the same experimental session, but in the presence of a different discriminative stimulus, responding either had no effect (extinction) or postponed delivery of an electric shock (avoidance). During sessions when the avoidance schedule was not in effect, d-amphetamine sulfate decreased punished responding. When the avoidance schedule was present during alternate 10 min periods, however, d-amphetamine markedly increased responding during punishment components. Increases in responding during avoidance components were also evident. The effects of d-amphetamine on punished responding depend on the context in which that responding occurs. 18 references. (Author abstract)

217545 Mertens, Henry W.; Steen, Jo Ann; Lewis, Mark F. Aviation Psychology Laboratory, FAA Civil Aeromedical Institute, Oklahoma City, OK 73125 **The effects of mevinphos on appetitive operant behavior in the gerbil.** Psychopharmacologia (Berlin). 41(1):47-52, 1975.

In a study of the effects on performance nonlethal organophosphate insecticide exposure, a different pair of gerbils served in each of the following schedules of reinforcement: fixed-ratio (FR) 25, FR 75, differential reinforcement of low rates (DRL) 12 sec, DRL 20 sec, and variable interval (VI) 1 min. Baseline performance in these tasks tended to be comparable to that of more common laboratory species, but was more variable in the case of the VI 1 min task. Mevinphos doses of 0.20mg/kg and above produced observable somatic signs of poisoning and also produced dose related decrements in performance in FR and VI tasks. Performance in the DRL schedule was affected only at a dose of 0.30mg/kg. No performance deficits or overt somatic signs of poisoning were present at mevinphos doses of 0.10mg/kg or lower. These results do not agree with those of an earlier study in which decrements in VI performance of pigeons and squirrel monkeys appeared at low mevinphos doses which did not produce overt somatic signs of poisoning. The possibility of variations in mevinphos effect as a function of species and task was discussed. 16 references. (Author abstract)

217547 Costall, B.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, West Yorkshire BD7 1DP, England **A comparison of circling models for the detectionparkinson activity.** Psychopharmacologia (Berlin). 41(1):57-64, 1975.

The effects of apomorphine, d-amphetamine, methylphenidate, nomifensine, ET495 and amantadine on stereotyped behavior in the rat was examined. L-Dopa was inactive in the absence of any pretreatment. The behavior induced by apomorphine, methylphenidate, nominfensine and amantadine persisted following pretreatment with alpha-methylparatyrosine. However, only the effect of apomorphine developed following combined pretreatment with reserpine alphalpha-methylparatyrosine. The effects of all stereotypic agents were inhibited by haloperidol, apomorphine, methylphenidate and nomifensine being most resistant. All agents, including L-Dopa, induced a dose dependent contralateral circling behavior in animals with asymmetric lesion of the medial raphe nucleus and a dose dependent ipsilateral circling after unilateral lesion of the substantia nigra. 30 references. (Author abstract modified)

217551 Freeman, J. J.; Choi, R. L.; Jenden, D. J. Department of Pharmacology, UCLA School of Medicine, Los Angeles, CA 90024 **The effect of hemicholinium on behavior and on brain acetylcholine and choline in the rat.** Psychopharmacology Communications. 1(1):15-27, 1975.

Behavior and whole brain acetylcholine and choline levels were studied in rats following intraventricular administration of hemicholinium-3. There was an 80% decrease in the content of acetylcholine after 2 hours. The depletion was associated with a decreased turnover of acetylcholine and aggressive behavior. The acetylcholine level did not return to control values until 72 hours after injection, when hemicholinium was still detectable as determinined by fluorescence assay. Endogenous choline levels were unaffected by hemicholinium; however, hemicholinium caused a significant reduction in the postmortem increase in choline. 7 references. (Author abstract modified)

217552 Robinson, R. G.; McHugh, P. R.; Bloom, F. E. Laboratory of Neuropharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Chlorpromazine induced hyperphagia in the rat.** Psychopharmacology Communications. 1(1):37-50, 1975.

In a study of chlorpromazine (CPZ) induced hyperphagia in the rat, during a 4 month period, 20 rats treated with subcutaneous injections of CPZ, at any dose tested, gained less weight than saline treated controls. However, increased feeding did occur on the first day of CPZ treatment if the animal was drug free for at least 2 days prior to treatment. The first day hyperphagia was a time limited response that did not occur until 8 hours after CPZ injection and lasted only 1 day.

During the period of hyperphagia, treated animals showed increased motivation to obtain food. Although sedation is a marked effect of CPZ and may be the reason for the delayed onset of hyperphagia, sedation with a different drug does not cause hyperphagia. It is suggested that accumulation of a metabolite of CPZ may interfere with the feeding response and cause the hyperphagia to disapper after the first day of treatment. 19 references. (Author abstract)

217652 Gogerty, J. H.; Penberthy, C.; Iorio, L. C.; Trapold, J. H. Pharmacology Section, Sandoz Pharmaceuticals, East Hanover, NJ 07936 **Pharmacological analysis of a new anorexic substance: 5-hydroxy-5-(4′-chlorophenyl)-2, 3-dihydro-5H-imidazo-(2, 1-a) isoindole (Mazindol).** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 214(2):285-307, 1975.

A pharmacological analysis of 5-hydroxy-5-(4′-chlorophenyl-2, 3-dihydro-5H-imidazo(2, 1-a)isoindole (Mazindol), a novel tricyclic compound is presented. The drug suppressed food consumption in rats at doses causing weak central stimulation and little effects on blood pressure or heartrate. The substance produced dose related decreases in the consumption of orange juice in cebus monkeys trained on an operant behavior schedule. The compound did not alter cardiac or pulmonary hemodynamics in the anesthetized dog but provided potentiation of norepinephrine pressor responses. Mazindol also demonstrated potent but incomplete antagonism of reserpine induced hypothermia in mice, antagonism of tetrabenazine catalepsy in rats, and suppression of mouse killing behavior of rats. Suppression of mouse killing was reduced by lesions placed in the septal area of the brain. Brain monoamine oxidase or catechol-O-methyltransferase activities were not altered. 33 references. (Author abstract modified)

217656 Ahlenius, S.; Engel, J.; Lundborg, P. Department of Pharmacology, University of Goteborg, Fack, S-40033 Goteborg 33, Sweden **Antagonism by d-amphetamine of learning deficits in rats induced by exposure to antipsychotic drugs during early postnatal life.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 288(2/3):185-193, 1975.

The acquisition of a conditioned avoidance response (CAR) was investigated in rats of nursing mothers given pimozide 0.5mg/kg on days 1, 2, 3, 4, 5, 6, and 7 after delivery. Four weeks after birth, the male littermates were tested for CAR acquisition in a two way avoidance situation or for correct CAR acquisition in a brightness discrimination situation. Offspring of mothers treated with pimozide were markedly inferior in the CAR acquisition in both behavioral situations as compared to those of mothers given glucose. The administration of d-amphetamine 15 min prior to the training session specifically counteracted the behavioral impairment obtained in the offspring of pimozide treated mothers. The results lend further support to the contention that the behavioral deficits in offspring of nursing mothers treated with neuroleptic agents are due to a developmental disturbance in central catecholamine neurons. 14 references. (Author abstract)

217660 Costall, Brenda; Naylor, Robert J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, Yorkshire, England **The behavioural effects of dopamine applied intracerebrally to areas of the mesolimbic system.** European Journal of Pharmacology (Amsterdam). 32(1):87-92, 1975.

The behavioral effects of dopamine applied intracerebrally to areas of the mesolimbic system were studied in the rat. The intracerebral injection was used to apply dopamine directly into dopamine containing areas of the mesolimbic system, the nucleus accumbens septi, tuberculum olfactorium and nucleus amygdaloideus centralis. Dopamine injected bilaterally into the nucleus accumbens septi caused a stereotyped sniffing behavior and hyperactivity but only a periodic hyperactivity developed after similar injections into the tuberculum olfactorium and no change in behavior was observed following injections into the nucleus amygdaloideeus centralis. After pretreatment with nialamide, the effects of intracerebral dopamine were enhanced. Dopamine injected into the tuberculum olfactorium caused a periodic biting behavior. Biting was not observed after injections into the nucleus accumbens septi and, even in the presence of nialmide, injections of dopamine into the nucleus amygdaloideus centralis failed to cause any change in motor behavior. 20 references. (Author abstract)

217670 Hodge, Gordon K.; Butcher, Larry L. Department of Psychology, University of California, Los Angeles, CA 90024 **Catecholamine correlates of isolation-induced aggression in mice.** European Journal of Pharmacology (Amsterdam). 31(1):81-93, 1975.

Drugs differentially affecting catecholaminergic neurotransmission mechanisms were injected into isolated mice to assess effects on aggression. L-DOPA in combination with a peripheral decarboxylase inhibitor produced a dose dependent decrease in the number of fights and average fight durations accompanied by an increase in attack latencies. Central dopamine levels were increased while brain noradrenaline and 5-hydroxytryptamine were reduced. Virtually identical effects on aggression were observed after apomorphine. Pimozide decreased fighting, but neither attack latencies nor average fight durations were affected. All doses of disulfiram virtually abolished all components of aggressive responses. The effect of D-amphetamine on number of fights was biphasic; lower doses potentiated aggression, but higher doses reduced fighting accompanied by increased attack latencies and reduced average fight durations. It is concluded that catecholamines may be intimately involved in mediating certain components of aggressive responses but that balance relationships among various putative neurotransmitters may be a more meaningful correlate of this behavior. 47 references. (Author abstract)

217671 Costall, Brenda; Naylor, Robert J.; Pinder, Roger M. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, Yorkshire, England **Dyskinetic phenomena caused by the intrastriatal injection of phenylethylamine, phenylpiperazine, tetrahydroisoquinoline and tetrahydronapthalene derivatives in the guinea pig.** European Journal of Pharmacology (Amsterdam). 31(1):94-109, 1975.

Dyskinetic phenomena caused by the intrastriatal injection of phenylethylamine, phenylpiperazine, tetrahydrosioquinoline and tetrahydronaphthalene derivatives in the guinea pig were examined. With the exception of the whole body and head and neck rocking movements the dyskinesias were specifically induced by dopamine like agents. The most conspicuous dyskinesias which followed the administration of phenylethylamine derivatives were the movements of biting, gnawing or locking and the development of marked locomotor hyperactivity. This effect was shown to be highly specific for dopamine. Of all compounds investigated 1-(3,4-dihydroxyphenyl)piperazine (DHPP) induced the most marked dyskinetic disturbances upon intrastriatal injection. Results are discussed in terms of the structure - activity relationships for the stimulation of different types of dopamine receptive structures within the neostriatum. 18 references. (Author abstract modified)

217675 Sahakian, B. J.; Robbins, T. W. Department of Experimental Psychology, University of Cambridge, Downing Street, Cambridge, CB2 3EB, England **Potentiation of locomotor activity and modification of stereotypy by starvation in apomorphine treated rats.** Neuropharmacology (Oxford). 14(4):251-257, 1975.

The effects of four levels of food deprivation were studied on locomotor and stereotypy responses of apomorphine injected rats. Locomotor activity with doses of 1-5mg/kg apomorphine was potentiated after 12, 24 and 72 hours of food deprivation. The stereotypy response with 1-5mg/kg apomorphine was modified by the deprivation, while the stereotypy response was enhanced with 0.5mg/kg apomorphine. The results are discussed in terms of the involvement of various possible behavioral and neurochemical mechanisms. 24 references. (Author abstract)

217765 Cappell, Howard; LeBlanc, A. E.; Herling, Seymore. Addiction Research Foundation, 33 Russell Street, Toronto, Ontario, M5S 2S1 **Modification of the punishing effects of psychoactive drugs in rats by previous drug experience.** Journal of Comparative & Physiological Psychology. 89(4):347-356, 1975.

Three experiments are described which examined the effects of history of chronic exposure to psychoactive drugs (amphetamine, morphine, and chlordiazepoxide) on aversive conditioning in rats by morphine and amphetamine. The findings are related to Parker, Failor, and Weidman's hypothesis, based on findings with morphine, concerning the development of conditioned preferences for substances associated with the repletion of artificially induced biological needs. It is suggested that the findings are best interpreted as a reflection of drug tolerance rather than conditioned preference. 18 references. (Author abstract modified)

217807 Fenwick, Shirlee; Mikulka, P. J.; Klein, Stephen B. Old Dominion University, Norfolk, VA 23508 **The effect of different levels of pre-exposure to sucrose on the acquisition and extinction of a conditioned aversion.** Behavioral Biology. 14(2):231-235, 1975.

The effect of preexposure on the rate of acquisition of a conditioned aversion and the effect of preexposure to sucrose on the extinction of a conditioned aversion in subjects taken to an identical acquisition criteria level were evaluated. Twenty eight female, water deprived rats were given 5 minutes preexposure access to sucrose for either 0, 6, 13, or 20 days. Beginning the following day, lithium chloride injections were given every third day until an aversion to the sucrose developed. The results indicate that as amount of preexposure to sucrose increased, it became increasingly more difficult to develop an aversion. Also, the rate of extinction of the conditioned aversion was directly related to amount of sucrose familiarization; increased familiarization facilitated extinction of aversion to sucrose. 8 references. (Author abstract modified)

217826 Muller, Pavel; Seeman, P. Pharmacology Department, University of Toronto, Toronto, Ontario, Canada M5S 1A8 **Neuroleptics: relation between cataleptic and anti-turning actions, and role of the cholinergic system.** Journal of Pharmacy and Pharmacology (London). 26(12):981-984, 1974.

The relationship between cataleptic and antiturning actions and the role of the cholinergic system was examined in rats. Chlorpromazine depressed the turning by 45% and 91% respectively. Thioridazine did not affect turning. The doses that decreased turning also induced statistically significant longer bar times, suggesting the presence of catalepsy. The results show that scopolamine completely blocked the catalepsy induced by chlorpromazine, and, at the same time, scopolamine antagonized (by 38%) the blockade of turning by chlorpromazine. The results indicate that the anticholinergic drugs antagonize the neuroleptic blockade of amphetamine induced turning. 21 references.

217828 Abel, E. L. Research Institute on Alcoholism, 1021 Main St., Buffalo, NY 14203 **Cannabis and aggression in animals.** Behavioral Biology. 14(1):1-20, 1975.

The effects of cannabis on aggressive behavior were examined. Irritable aggression tends to be increased by cannabis whereas predatory and intermale aggression tend to be reduced. If aggressive behavior is examined in these terms, then cannabis is seen to have a differential rather than a dual effect on aggression in animals. 98 references. (Author abstract)

217829 Masur, Jandira; Maroni, J. B.; Benedito, Marco A. C. Departamento de Psicobiologia, Escola Paulista de Medicina, Rua Botucatu, 862-04023, Sao Paulo, Brasil **Genetically selected winner and loser rats in the tunnel competition: influence of apomorphine and dopa.** Behavioral Biology. 14(1):21-30, 1975.

The effects of apomorphine, dopa and haloperidol on the competitive behavior in a straight runway of genetically selected winner runway rats (WRS rats), loser runway rats (LRS) and nonselected rats were studied. Apomorphine significantly increased the percentage of winning in nonselected rats competing against WRS rats. In another experiment LRS rats which lost 100% of the contests aginst WRS rats, achieved 50-60% of wins when under apomorphine or dopa effects. When retested without drugs they were again defeated. In pairs made up of two nonselected rats, haloperidol blocked the increase of winning induced by apomorphine. Use of the terms winning and losing instead of dominance and submission to describe the competitive behavior of rats in the straight runway is discussed. 13 references. (Author abstract)

217833 Buckholtz, Neil S. Department of Biochemistry, Medical University of South Carolina, Charleston, SC 29401 **6-Methoxy-1,2,3,4-tetrahydro-beta-carboline produces a retention deficit for one-trial passive-avoidance in mice.** Behavioral Biology. 14(1):95-101, 1975.

The effects of 6-methoxy-1,2,3,4-tetrahydro-beta-carboline (6-Me0-THBC) were tested on one trial passive-avoidance behavior in CF1 mice. Animals which received 6-Me0-THBC 2 hr prior to training had increased latencies compared to saline controls during initial entrance into the shock compartment but had decreased latencies during a retention test 24 hr later regardless of whether they had received footshock or not during initial training. However, 50mg/kg 6-Me0-THBC produced a decreased retention latency only for the group that received footshock and had no effect on training latencies. 6-Me0-THBC given immediately after the training trial had no effect on retention. 6-Me0-THBC (100 mg/kg) did not affect the animals' response to shock. Brain serotonin was increased 2 hr after this dose but returned to control levels 24 hr later. There may therefore, be a relationship between increased brain serotonin and a deficit in retention of one trial passive-avoidance. 22 references. (Author abstract)

217835 Stromberg, Ulf; Svensson, Torgny H. Department of Pharmacology, University of Goteborg, Fack, S-400 33

Goteborg 33, Sweden **Differences between (+)- and (-)-amphetamine in effects on locomotor activity and L-Dopa potentiating action in mice.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 287(2):171-179, 1975.

The L-Dopa potentiating effects of the two optical isomers of amphetamine, as well as the effects of their own, were investigated in mice, using locomotor activity as a test parameter. The time courses were studied for the effects of (+)-amphetamine and (-)-amphetamine and L-Dopa. Dose response relationships were established for the amphetamine enantiomers. The L-Dopa potentiating effects, of a few, selected doses of the amphetamine isomers were investigated by establishing dose response curves for L-Dopa with and without the amphetamines. (+)-Amphetamine caused a dose dependent stimulation of locomotor activity, whereas (-)-amphetamine caused a dose dependent depression. Doses higher than 8mgkg of the laevo isomer caused stimulation of the activity. (+)-Amphetamine and (-)-amphetamine doses without any effect on locomotor activity of their own, caused virtually the same shift to the left of the dose - response curve for L-Dopa. (-)-Amphetamine which per se caused depression of locomotor activity, caused a marked potentiation of the L-Dopa induced stimulation of motor activity. Thus, there does not exist a close correlation between the L-Dopa potentiating action of the amphetamines and their stimulating properties. 15 references. (Author abstract modified)

217846 Cervantes, Miguel; De La Torre, Laura; Beyer, Carlos. Departmento de Investigacion Cientifica, Instituto Mexicano del Seguro Social, Apartado Postal, 73-032, Mexico 73 D.F. **Analysis of various factors involved in EEG synchronization during milk drinking in the cat.** Brain Research (Amsterdam). 91(1):89-98, 1975.

Electroencephalographic (EEG) and multineuronal activity (MUA) from several brain structures were recorded in 11 adult cats during milk drinking. Milk drinking elicited parietal and hippocampal EEG synchronization and inhibited multiunit discharge in several brain regions. The proportion of EEG synchronization varied considerably between animals, but remained more or less constant for each cat after several testing days. Neither modification of milk concentration nor fasting influenced the proportions of EEG synchronization during milk drinking. Adaptation of the animals to the experimental environment facilitated the appearance of EEG synchronization during milk drinking. Chlorpromazine significantly increased the proportion of EEG synchronization observed during milk drinking. By contrast, displacement of the head, neck or postural body adjustments during milk drinking blocked EEG synchronization. Amphetamine also had a suppressive effect on the EEG parietal and hippocampal synchronic activity observed during milk drinking. Results suggest that development of parietal EEG synchronization in response to pleasant stimulation is a complex phenomenon requiring a relaxed condition of the animal, including its adaptation to the experimental environment and relative immobility with the concomitant diminution of afferent inflow from some of the muscles involved in locomotion. 21 references. (Author abstract)

217856 Gradwell, P. B.; Everitt, B. J.; Herbert, J. Department of Anatomy, University of Rhodesia, Salisbury, Rhodesia **5-Hydroxytryptamine in the central nervous system and sexual receptivity of female rhesus monkeys.** Brain Research (Amsterdam). 88(2):281-293, 1975.

The role of 5-Hydroxytryptamine (5-HT) in the control of sexual receptivity in female rhesus monkeys was studied in 24 adult females paired with six adult males. p-Chlorophenylalanine (PCPA), a selective inhibitor of 5-HT, was found to reverse unreceptivity induced by adrenalectomy in ovariectomized, estrogen treated females. PCPA treated females presented more frequently and initiated more sexual behavior, or else they refused fewer of the male's attempts to mount. These effects were in turn reversed by 5-hydroxytryptophan (5-HTP) when this was given to PCPA treated animals. In addition, 5-HTP given alone to ovariectomized estrogen treated females reduced their receptivity. Parallel biochemical experiments showed that PCPA in the doses used lowered the levels of 5-HT in the brain as measured by the levels of 5-hydroxyindole-3-acetic acid (5-HIAA) in the cerebrospinal fluid, and that these were restored by 5-HTP. Both estradiol benzoate and testosterone propionate lowered the turnover rates of 5-HT in the brain (as measured by the probenecid test) in ovariectomized female monkeys. 55 references. (Author abstract modified)

217883 Leshem, M. B.; Blundell, J. E. Psychology Department, Leeds University, Leeds LS2 9JT, England **Interactive effect of (plus/minus)-fenfluramine and (+)-amphetamine on feeding in rats.** Journal of Pharmacy and Pharmacology (London). 26(11):905-906, 1974.

The interactive effect of fenfluramine and (+)-amphetamine on feeding in rats was examined. The results show that amphetamine and fenfluramine, when injected alone, give rise to a dose dependent reduction in food intake. The most profound effect on feeding was observed after the administration of the smallest doses of amphetamine and fenfluramine in combination. This finding shows that fenfluramine does not antagonize the anorexic action of amphetamine, nor is there competitive inhibition between the anorexic effects of the two drugs. On the contrary, the anorexic effects of amphetamine and fenfluramine appear to summate, a finding consistent with the belief that the drugs exert selective effects on different components of the brain amine systems involved in the regulation of feeding. 10 references.

218115 Klawans, Harold L.; Margolin, David I. Michael Reese Medical Center, 29th St. and Ellis Ave., Chicago, IL 60616 **Amphetamine-induced dopaminergic hypersensitivity in guinea pigs: implications in psychosis and human movement disorders.** Archives of General Psychiatry. 32(6):725-732, 1975.

The effect of chronic amphetamine pretreatment on amphetamine induced stereotyped behavior was studied in guinea-pigs. Following chronic amphetamine pretreatment, animals demonstrated an increased sensitivity to both d-amphetamine sulfate and apomorphine hydrochloride induced stereotyped behavior. This observation suggests that chronic exposure to high doses of a dopamine agonist (d-amphetamine) alters the response of the brain to the subsequent administration of both indirect (d-amphetamine) and direct (apomorphine) dopamine agonists. This altered response may be due to the development of dopamine receptor site supersensitivity. Clinical evidence suggests that a similar agonist induced hypersensitivity may play a role in the development of dyskinetic movement disorders and psychoses in humans following the chronic use of such dopamine agonists as amphetamine and levodopa. 48 references. (Author abstract modified)

218364 Kawa, Akira; Kawano, Michio; Uchimura, Hayato. First Department of Internal Medicine, Kagoshima Univ. School of Medicine, Usuki 1201-1, Kagoshima City, 892 Japan **Role of brain serotonin in the integration of behavioral responses and pituitary-adrenocortical functions under emotion.** Jour-

nal of Japanese Psychosomatic Society (Fukuoka). 15(1):10-17, 1975.

The role of brain amines in the integration of behavioral and pituitary - adrenocortical functions under stress was studied clinically and experimentally. Immobilization resulted initially in a decrease of brain noradrenaline and an increase in plasma corticosterone, and in the decrease of both upon repetition of immobilization in rats. In conditioned avoidance elaborated in rats, nonlearners, exposed to chronic psychic stress, showed the significant increase in hypothalamic noradrenaline. Depletion of brain noradrenaline following administration of 6-hydroxydopamine resulted in the suppression of rearing and the facilitation of defense aggressiveness. Results demonstrate the importance of brain noradrenaline in the regulation of behavioral responses under stress. There is no evidence for the control of pituitary - adrenocortical function by brain noradrenaline in any aspect of resting level, feedback mechanism or of the response to stressors. Psychoactive drug, FK-880 (sulpiride), showed a tranquilizing effect in double-blind tirals. 43 references. (Journal abstract modified)

218470 Zin'kovskaya, L. Ya.; Komissarov, I. V.; Tikhonov, V. N. Donetskogo meditsinskogo instituta im. A. M. Gor'kogo, Donetsk, U.S.S.R. **/The influence of lithium and cesium ions on the effects of catecholamines and serotonin introduced into the hippocampus of rats./** O vliyanii ionov litiya i tseziya na effekty katekholaminov i serotonina, vvodimykh v gippokamp krys. Farmakologiya i toksikologiya (Moskva). 38(2):135-137, 1975.

The influence of lithium and cesium ions on the effects of dopamine, norepinephrine and serotonin injected into the dorsal hippocampus was investigated in 18 rats. Local microinjections of the catecholamines and serotonin affected neither muscle tone nor spontaneous motor activity, but did lengthen the latent period of a conditioned avoidance reflex (CAR). Following preliminary injection of lithium chloride, dopamine had a strong inhibitory effect on the CAR and stimulated motor activity. Preliminary lithium chloride injections did not influence the action of norepinephrine and serotonin on the length of the CAR latent period, but it did cause norepinephrine to depress motor activity. An explanation for the mechanisms of ion influence was concluded to require further investigation. 10 references. (Journal abstract modified)

218471 Gromov, A. I. Moskovskogo meditsinskogo instituta im. I. M. Sechenova, Moscow **/The participation of cerbral cholinergic mechanisms in the action of neuroleptics./** Uchastiye kholinergicheskikh mekhanizmov mozga v deystvii neyroleptikov. Farmakologiya i toksikologiya (Moskva). 38(2):145-148, 1975.

The participation of the muscarinic cholinopositive component in the neuroleptically induced emotional reactions of fear and aggression was investigated in 520 albino mice. Emotional thresholds of fear and aggression were evoked by painful electrical stimulation. The neuroleptics droperidol, haloperidol and ethaperazine were found to subdue the aggressive reaction while increasing the sensitivity of the muscarinic cholinoreactive systems to the tremor inducing effect of arecoline. Neuroleptic inhibition of fear was insignificant. Amizyl and cyclodol eliminated the muscarinic cholinopositive action of the neuroleptics, thereby greatly reducing their antiaggressive activity. Muscarinic cholinergic activation was concluded to play a decisive role in neuroleptic antiaggressive activity. 10 references. (Journal abstract modified)

218472 Popova, N. K.; Bertogayeva, V. D. Laboratoriya populyatsionnoy farmakologii Instituta tsitologii i genetiki Sibirskogo otdeleniya AN SSSR, Novosibirsk, U.S.S.R. **/The participation of serotonin reactive brain structures in some forms of behavioral patterns in hamsters./** Ob uchastii serotoninoreaktivnykh struktur mozga v nekotorykh formakh povedeniya zolotistykh khomyakov. Farmakologiya i toksikologiya (Moskva). 38(2):148-150, 1975.

The participation of serotonin sensitive structures in behavioral patterns of hamsters was investigated during playful activity, slumber, aggressive behavior, and stress conditions arising from grouping adult male hamsters together. Serotonin level in the brainstem was found to drop during playful activity and rise during subsequent slumber. No change was noted in the corticosteroid content of peripheral blood during play. Ipramizid and 5-hydroxytryptophan inhibited playful activity, while deoxyphenylalanine did not influence it. Similar depression of the serotonin level in the brainstem was noted during aggressive behavior and stress conditions. Changes in the brainstem serotonin content were concluded not to be associated with emotional coloration, but rather to reflect the transition from somnolence to highly active behavior. 11 references. (Journal abstract modified)

218492 Mulick, James A.; Joffe, J. M.; Peterson, John M. Dept. of Psychology, Univ. of Vermont, Burlington, VT 05401 **Sex differences in the effects of dexamethasone phosphate on behavior in rats.** Physiology & Behavior. 14(1):37-42, 1975.

The effect of dexamethasone phosphate (DEX) administration in rats' drinking water on running activity and open field behavior was examined. In Exp 1 males were given DEX continuously from either 5 days or 1 day prior to and throughout testing. Only 5 day treatment significantly increased running wheel activity. DEX had no significant effect on males' 4 day open field activity but significantly reduced open field and home cage defecation. In Exp 2 females given DEX defecated significantly more in the open field than controls. The effect on females does not appear to be due to a general metabolic change since DEX females, like males, defecated significantly less than controls in the home cages. Females' open field activity was not significantly affected. Weight loss and plasma corticosterone analysis confirmed the effectiveness of the dosage used. The sex differences in the effects of DEX on open field defecation is possibly due to interaction with gonadal hormones. 24 references. (Author abstract)

218498 Mabry, Paul D.; Campbell, Byron A. Dept. of Psychology, Princeton Univ., Princeton, NJ 08540 **Potentiation of amphetamine-induced arousal by food deprivation: effect of hypothalamic lesions.** Physiology & Behavior. 14(1):85-88, 1975.

The effect of hypothalamic lesions on the amphetamine deprivation interaction in stabilimeters was examined in rats. Locomotor activity was studied in rats with lesions of the basomedial hypothalamus (BMH) following food deprivation and amphetamine. Controls showed the normal potentiation of amphetamine induced locomotor activity by starvation. Animals with lesions did not differ, when deprived, from satiated control animals in their response to amphetamine. Results suggest that the behavioral arousal produced by food deprivation is mediated by the BMH. 21 references. (Author abstract modified)

218800 Poshivalov, V. P. Pervyy Leningradskiy meditsinskiy institut im. I. P. Pavlova, Leningrad **/A pharmacological analysis of aggressive behavior of mice induced by isolation./** Farmakologicheskiy analiz agressivnogo povedeniya myshey, vyzvannogo izolyatsiyey. Zhurnal vysshey nervnoy deyatel'nosti imeni I. P. Pavlova (Moskva). 24(5):1079-1081, 1974.

The effect of neuroleptics and analgesics on separate psychological components of aggressive behavior elicited by social isolation was investigated in mice. Behavior was measured both prior to and following drug injections. Levels of aggressive behavior were found to depend upon length of time in isolation. Aminazine and droperidol had an antiaggressive effect on the mice; the longer the time spent in isolation, the larger the doses needed to suppress aggression. 5 references.

218803 Talalayenko, A. N. Donetskogo meditsinskogo instituta im. A. M. Gor'kogo, Donets, U.S.S.R. /**On neurochemical mechanisms of septum influence on the conditioned avoidance reaction in rats.**/ O neyrokhimicheskikh mekhanizmakh vliyaniya peregorodki na uslovnuyu reaktsiyu izbeganiya krys. Zhrunal vysshey nervnoy deyatel'nosti imeni I. P. Pavlova (Moskva). 24(4):708-715, 1974.

The influence of microinjections of monoamines and amino acid into the lateral nuclei of the septum on conditioned avoidance reactions was investigated in rats. Noradrenaline was found to considerably increase reflex latency and to stimulate spontaneous motor activity. These effects were mediated through the alpha-adrenoreceptors of the septum neuronal systems. Dopamine diminished and serotonin and L-glutamate increased reflex latency, without affecting muscular tone or motor activity. Dopamine influences were mediated through septum neural structures sensitive to haloperidol, chlorpromazine and deseril; serotonin effects were mediated through D-serotonin lateral septum receptors. The action of L-glutamate on the conditioned defense reflex was not linked with its action on adrenergic, dopaminegic, or serotonergic biochemical systems of the septum units. 35 references. (Journal abstract modifie)

218814 Burov, Yu. V.; Salimov, R. M. Laboratoriya farmakoterapii ekstermal'nykh sostoyaniy, Instituta farmakologii AMN SSSR, Moscow /**The influence of pharmacological agents on the consequences of emotional excitation in cats.**/ Vliyaniye farmakologicheskikh veshchest na posledstviya emotsional'nogo vozbuzhdeniya u koshek. Zhurnal vysshey nervnoy deyatel'nosti imeni I. P. Pavlova (Moskva). 24(4):825-832, 1974.

The effect of pharmacological agents on behavioral changes following fear and rage reactions elicited by electrical stimulation of the anterior hypothalamus was investigated in cats. The frequency of individual motor acts was recorded. The general result of emotional fear and rage reactions was suppression of orientation and attention. Stelazine, haloperidol, amitriptyline, imipramine, chlordiazepoxide, diazepam and benactyzine prevented suppression of orientation and attention. Complete normalization of all behavioral parameters was manifested only after diazepam and benactyzine administration. Chlorpromazine did not affect the consequences of emotional rage, but exacerbated the consequences of the fear reaction. The muscarinic cholinergic structures of the hypothalamus were concluded to participate in the development of the emotional reactions of rage and fear. 24 references. (Journal abstract modified)

218954 Baltzer, Victor; Weiskrantz, Lawrence. Biological Research Laboratories, Pharmaceuticals Division, CIBA-GEIGY Limited, Basle, Switzerland **Antidepressant agents and reversal of diurnal activity cycles in the rat.** Biological Psychiatry. 10(2):199-209, 1975.

The locomotor activity of rats was studied before and after reversal of the daily light - dark cycle, combined with treatment by three antidepressant drugs, two neuroleptics, one anxiolytic, one stimulant, or saline. The relative distribution of activity of rats treated with the antidepressant drugs, but not with other drugs, returned to prereversal patterns significantly more closely than that of saline controls. The results are discussed in connection with the observation of disturbance of diurnal rhythms in depressed patients. 23 references. (Author abstract)

219020 Downey, Danniel J. University of Arizona, Tucson, AZ 85721 **State-dependent learning with centrally and noncentrally active drugs.** Bulletin of the Psychonomic Society. 5(4):281-284, 1975.

The ability of a drug without direct CNS activities to produce dissociation in a nondifferential responses (conditioned avoidance) task was investigated. Holtzman rats performed in a simple switchback, transfer of training paradigm in which all four possible combinations of drug and nondrug were represented. Drug states were produced by injection of chlorpromazine hydrochloride, sodium pentobarbital, or l-epinephrine. Results indicate that only with centrally active chlorpromazine and pentobarbital could any appreciable dissociation be obtained. No dissociation was obtained with the ANS stimulant, l-epinephrine. It is concluded that the production of state dependent learning involving a unitary response depends on direct action of a drug on the CNS. 16 references. (Author abstract modified)

219023 Ternes, Joseph W. Carribbean Primate Research Center, University of Puerto Rico, Sabana Seca, Puerto Rico 00794 **Conditioned aversion to morphine with naloxone.** Bulletin of the Psychonomic Society. 5(4):292-294, 1975.

The use of naloxone to condition aversions to morphine in dependent rats which were accustomed to self-administer their daily dose by drinking weak morphinized solutions was investigated. Following an 8 day two bottle test during which the Ss demonstrated that they had acquired a preference for morphine over water, morphine injection was substituted for morphine solution for 7 days. Morphine solution was then paired with injection of naloxone in the experimental group and physiological saline in the control group. Subsequently a two bottle preference test between morphine solution and water was given for 6 days. Maintenance during this extinction period involved either daily injection of morphine in experimental and control subgroups or daily injection of physiological saline in the second experimental and control subgroups. Results indicate that a profound aversion to morphine is conditionable in the experimental group regardless of whether the urgency to drink morphine to relieve withdrawal stress is controlled. 10 references. (Author abstract modified)

219031 Ternes, Joseph W. Caribbean Primate Research Center, University of Puerto Rico, Sabana Seca, Puerto Rico 00794 **Naloxone-induced aversion to sucrose in morphine-dependent rats.** Bulletin of the Psychonomic Society. 5(4):311-312, 1975.

Naloxone induced aversion to sucrose in morphine dependent rats was investigated. Two groups of Wistar rats, morphine dependent and controls, were given 4% sucrose solution to drink for 15 min followed by intramuscular injection with naloxone. Morphine dependent Ss showed a marked aversion to sweet water in a postconditioning two bottle preference test. Control Ss preferred the sucrose solution. The results suggest that naloxone induced taste aversion can provide a useful measure of morphine dependency. 7 references. (Author abstract)

219032 Houser, Vincent P. Psychotropic Drug Laboratory, Veterans Administration Hospital, Perry Point, MD 21902 **Effects of chronic administration and withdrawal of d-amphetamine upon daily activity levels of squirrel monkeys.** Bulletin of the Psychonomic Society. 5(4):313-314, 1975.

The effects of chronic administration and withdrawal of d-amphetamine sulfate on the activity of squirrel monkeys in a modified Sidman avoidance schedule were investigated. Two squirrel monkeys were placed in activity cages for a 7 week experimental period. Activity levels were recorded every hour 24h a day. Animals received daily injections of d-amphetamine sulfate for 7 consecutive days followed by 14 days of saline administration. Both dosages of amphetamine were able to reliably elevate mean activity levels during the 12h after drug administration. During the drug withdrawal periods animals demonstrated significant decrements in baseline activity levels. These effects indicate that chronic amphetamine administration does produce long lasting biochemical changes in the central nervous system of the squirrel monkey which are reflected by the decreased motor activity noted after the drug is withdrawn. 6 references. (Author abstract)

219033 Ternes, Joseph W. Caribbean Primate Research Center, University of Puerto Rico, Sabana Seco, Puerto Rico 00794 **Induced preference for morphine in rats.** Bulletin of the Psychonomic Society. 5(4):315-316, 1975.

A simple procedure for the induction of morphine dependency in rats is described. Two groups of 15 Wistar rats were given weak solutions of morphine in water as their only source of liquid for either 84 or 60 days. Subsequently, both groups were given a two bottle preference test between morphine solution and vehicle for 8 days. Results indicate a higher level of fluid intake in the 84 day group. Both groups drank more than 50% of their total fluid intake in the form of morphine solution, however, only the mean of 84 day exposure group was significantly different from 50%. It is concluded that morphine dependency can be induced by forcing consumption of weak solutions of morphine for 12 weeks. The results are discussed as an example of unprepared learning. 16 references. (Author abstract)

219039 Fernandez, B.; Ternes, J. W. Caribbean Primate Research Center, University of Puerto Rico, Sabana Seca, Puerto Rico 0079[illegible] **Conditioned aversion to morphine with lithium chloride in morphine-dependent rats.** Bulletin of the Psychonomic Society. 5(4):331-332, 1975.

The hypothesis that conditioned aversion can be used as a method for weaning morphine dependent rats from their drug was tested. Two groups of Wistar rats which had learned to drink morphine solution in order to avoid withdrawal stress received two separate pairings of morphine taste with either intraperitoneal injection of LiCl or physiological saline. A two bottle extinction test between morphine solution and tap water was given on the day separating the two conditioning trials and for 4 days following the second conditioning trial. An ANOVA indicate no significant main effects; however, the Groups by Days interaction was significant. Test of simple main effects of groups were significant on the days following each conditioning trial. Long-term familiarity with the test substance did not block conditioning. The results are discussed as an example of prepared learning. 8 references. (Author abstract)

219069 Siegel, Harold I.; Rosenblatt, Jay S. Department of Obstetrics and Gynecology, Kansas University Medical Center, Kansas City, KS 66103 **Estrogen-induced maternal behavior in hysterectomized-ovariectomized virgin rats.** Physiology & Behavior. 14(4):465-471, 1975.

The effectiveness of estrogen and estrogen in combination with progesterone in stimulating the onset of short latency maternal behavior in hysterectomized - ovariectomized virgin female rats was investigated. A single injection of 100micrograms/kg estradiol benzoate (EB) either alone or in combination with 0.5mg progesterone resulted in a significant reduction in the latency for onset of maternal behavior in hysterectomized - ovariectomized virgin rats as compared to the latencies of groups which either remained intact or were subjected to alternative surgical procedures or different doses of EB. There was no shortening of the maternal latencies when ovariectomy or combined hysterectomy - ovariectomy was performed 8 weeks prior to testing while the administration of EB 8 weeks postoperatively was still effective in stimulating short latency maternal care in hysterectomized - ovariectomized females and increased the percentage of ovariectomized sham hysterectomized maternal responses. It is concluded that estrogen is capable of inducing maternal behavior in virgin rats and that the uterus plays an important, but undetermined, role. 30 references. (Author abstract modified)

219070 Siegel, Harold I.; Rosenblatt, Jay S. Department of Obstetrics and Gynecology, Kansas University Medical Center, Kansas City, KS 66103 **Latency and duration of estrogen induction of maternal behavior in hysterectomized-ovariectomized virgin rats: effects of pup stimulation.** Physiology & Behavior. 14(4):473-476, 1975.

Shortened latencies for the onset of maternal behavior in estrogen treated hysterectomized - ovariectomized female rats as a result of earlier exposure to pups were investigated, and the longevity of the effects of a single estrogen injection was assessed. The latency for the onset of maternal behavior was measured in virgin rats which received either 100micrograms/kg estradiol benzoate (EB) or oil immediately following ovariectomy and hysterectomy. Different groups of EB and oil treated females were presented with 3-8-day-old pups at 0 hr, 24 hr, and 48 hr after their injections. Only the females given EB exhibited short latency maternal behavior; latencies as short as 24 hr were observed in 46% of the animals which were presented with pups at 0 hr and within 48 hr, 92% of the group were maternal. The effects of EB on maternal responsiveness could be detected between 48 hr to 72 hr after injection, effects equal to those occurring over the first and second 24 hr periods. 13 references. (Author abstract)

219071 Weiss, Charles S.; Almli, C. Robert. Department of Psychology, Ohio University, Athens, OH 45701 **Polyethylene glycol induced thirst: a dual stimulatory mechanism?** Physiology & Behavior. 14(4):477-481, 1975.

The dipsogenic properties of polyethylene glycol (PG) treatment were evaluated by measuring drinking behaviors and serum conditions following PG treatment. Hyperoncotic colloid dialysis with PG resulted in significant water intakes for rats within 1 hr posttreatment, when water was made immediately available. Associated with reliable drinking were azotemia (52%) and hypernatremia (6%), but not hypovolemia. When PG treated rats were delayed without food - water for 6 hr post PG treatment, the greatest volumes of water were consumed and the rats were both azotemic (111%) and hypovolemic (11%-25%). The dipsogenic properties of urea were tested and demonstrated. The combined data suggest that PG treatment stimulates thirst via cellular and extracellular mechanisms. 20 references. (Author abstract)

219073 Panksepp, Jaak; Pollack, Alan; Krost, Kathleen; Meeker, Rick; Ritter, Michael. Department of Psychology,

Bowling Green State University, Bowling Green, OH 43404 **Feeding in response to repeated protamine zinc insulin injections.** Physiology & Behavior. 14(4):487-493, 1975.

Feeding changes in response to repeated daily injections of protamine zinc insulin were studied. Sustained overeating was induced in rats with repeated daily injections of protamine zinc insulin. The hyperphagia and hypophagia upon termination of insulin treatment were directly related to the amount of insulin that had been administered. The intake was regulatory since animals adjusted food consumption appropriately to compensate for caloric intake from glucose solutions, and they maintained stable caloric intake by reducing the weight of food ingested from a high fat diet. Overeating was unmodified by the use of an equicaloric high protein diet even though total weight gain was reduced. Injections of cycloheximide and dexamethasone prevented protamine zinc insulin induced overeating. 31 references. (Author abstract)

219075 Leroux, A. G.; Myers, R. D. Department of Psychology, University of the North, Pietersburg, South Africa **Action of serotonin microinjected into hypothalamic sites at which electrical stimulation produced aversive responses in the rat.** Physiology & Behavior. 14(4):501-505, 1975.

The role of serotonergic neurons in the hypothalamus in aversive behavior was studied through the injection of 5-hydroxytryptamine (5-HT) via bipolar chemitrode. A bipolar chemitrode was implanted in male rats subsequently trained to avoid an aversive electrical stimulus by depressing a lever. Microinjections in a volume of 0.4microliters to 0.7microliters of an artificial CSF solution or of doses of 1.0microgram or 5.0micrograms of acetylcholine, dopamine or norepinephrine into the neuron mass directly at the tip of the electrode failed to alter the rate of avoidance responding to the electrical stimulation. However, 5-HT microinjected similarly in a dose of 5.0micrograms at the tip of the electrode caused a fourfold increase in the acceptance of aversive electrical stimulation. It is concluded that serotonergic neurons function to attenuate punishing stimuli within the negatively reinforcing pathways located in the diencephalon. 23 references. (Author abstract modified)

219083 Wilson, J. Roger; Dicara, Leo V. Mental Health Research Institute, University of Michigan, Ann Arbor, MI 48104 **Effects of previous curare-immobilization on Pavlovian conditioned heart decelerations in the curarized rat.** Physiology & Behavior. 14(3):259-264, 1975.

Two experiments were conducted to determine if repeated d-tubocurarine chloride (dTC) paralysis facilitates acquisition of a Pavlovian heartrate (HR) conditioning in the dTC paralyzed rat. In experiment one, Pavlovian HR conditioning was examined in curarized rats which had (1) experience with dTC induced immobilization before conditioning, or (2) no experience with dTC induced immobilization. The results show that pronounced conditioned HR decelerations were observed only for the curare experienced animals. Experiment two was conducted to determine if repeated curarization influenced tolerance to dTC induced neuromuscular paralysis. No group differences in basal electromyographic (EMG) activity or time to recover from paralysis were found between the noncurare adapted and the curare adapted groups. The implications of the results are discussed in terms of the role of immobilization induced stress on acquiring stimulus control over automatic responses. 24 references. (Author abstract modified)

219110 Popova, N. K.; Nikulina, E. M.; Arav, V. I.; Kudryavtseva, N. N. Laboratoriya populyatsionnoy farmakologii, Instituta tsitologii i genetiki Sibirskogo otdeleniya AN SSSR, Novosibirsk, U.S.S.R. **/On the role of serotonin in predatory aggression./** O roli serotonina v odnom iz vidov agressivnogo povedeniya "agressii khishchnika". Fiziologicheskiy zhurnal SSSR imeni I. M. Sechenova (Leningrad). 61(2):183-186, 1975.

The role of serotonin in controlling the mouse killing instinct was investigated in rats. Electrolytic lesions of the midbrain raphe nuclei lowered the serotonin level in the forebrain, thus eliciting mouse killing behavior. After lesion, 50% of previously nonkiller rats became mouse killers. 5-Hydroxytryptophan administration elevated serotonin levels to normal values and completely blocked predatory aggression. Administration of p-chlorophenylalanine reduced cerebral serotonin level and slightly stimulated aggressive behavior. Brain serotonin was concluded to be an inhibitory factor in the mouse killing behavior of rats. 17 references. (Journal abstract modified)

219268 Harrell, Lindy E. University of Massachusetts **Recovery of function: some new thoughts on an old problem. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-6034 HC$13.50 MF$5.00 64 p.

Recovery of function following brain damage was studied and some new thoughts are offered on possible ways of modifying the consequences of brain surery by certain presurgical and postsurgical treatments. Presurgical treatment with insulin or glucagon 5 days prior to lesions of the lateral hypothalamus shortened or lengthened, respectively, the aphagic period brought about by this type of lesion (experiment one). Experiment two demonstrated that the aphagic period following lateral hypothalamic lesions could be abbreviated by electrical stimulation in the lesioned area. To generalize the phenomenon, the effect of paracholorophenylalanine pretreatment on septal rage was studied in experiment three. Reduction in the rage syndrome was produced by 5 day pretreatment, but not with 2 day pretreatment or with 5 day pretreatment with insulin. Experiment four examined the effects of environmental illumination on the motor impairments consequent to lateral hypothalamic lesions. Overall findings suggest that the pretreatment and posttreatment modified the levels of certain neurotransmitters, which, in turn, caused the alteration of the recovery period. (Journal abstract modified)

219278 Quenzer, Linda Frances. University of Massachusetts **Examination of the role of brain amines and cyclic AMP in benzodiazepine-induced suppression of aggression. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-6072 HC$13.50 MF$5.00 66 p.

The role of brain amines and cyclic 3′,5′-adenosine monophosphate (cyclic-AMP) in benzodiazepine induced suppression of aggression was studied to test an alternate hypothesis which suggests that phosphodiesterase inhibition may be the cause of the reduction of shock induced aggression (SIA) observed in previous studies of the depressant effects of chlordiazepoxide (CDP). A phosphodiesterase stimulator, imidazole acetic acid, had no effect on SIA alone, but when administered with CDP reduced it further, rather than increasing the level of fighting. While CDP reduced septal lesion induced rage, pretreatment before lesioning did not alter the effectiveness of the drug. Thus, it seems that the attenuation of septal rage is neither dependent on the adrenergically mediated behavioral depressant effect of CDP, nor could any serotonergic mechanism be reliably related to the effect. A more specific antiaggression effect is suspected. (Journal abstract modified)

219289 Jaso, John Joseph. University of Oklahoma **Hippocampal and pituitary-adrenal influences on activity and avoidance behavior. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-6526 HC$13.50 MF$5.00 75 p.

The effects of hippocampal lesions in male albino rats were examined under pharmacologically induced changes in pituary - adrenal function to determine whether the behavioral changes produced by these lesions are the result of elevated pituitary - adrenal activity. Ss were tested on activity, passive-avoidance and active avoidance under saline conditions and after administration of dexamethasone, a synthetic corticoid which suppresses adrenocorticotropic hormone (ACTH). Overall findings point to specific and nonspecific effects of hippocampal lesions. The passive-avoidance retention deficit observed after lesioning is apparently related to the disruption of normal hippocampal function. The observed activity and active avoidance behavior are attributed to alterations in pituitary - adrenocortical function that have been reported subsequent to hippocampal lesions. (Journal abstract modified)

219327 Mityushov, M. I.; Sokolova, Ye. V. Laboratoriya eksperimental'noy endokrinologii Instituta fiziologii im. I. P. Pavlova AN SSSR, Leningrad **/The influence of hydrocortisone on the elaboration of extinction inhibition in rats./** Vliyaniye gidrokortizona na vyrabotku ugasatel'nogo tormozheniya u krys. Zhurnal vysshey nervnoy deyatel'nosti imeni I. P. Pavlova (Moskva). 24(6):1222-1226, 1974.

The influence of hydrocortisone on the extinction of defensive conditioned reflexes elaborated by the unilateral avoidance method was investigated in male rats. Following hydrocortisone administration, the magnitude of deviations of the average number of conditioned reflexes in the experimental group was compared with the corresponding value in the control group. Hydrocortisone administration 30 minutes before the start of the experiment in doses of 5mg per 100gm was found to result in a positive value of the average deviation, indicating a significant delay in extinction inhibition elaboration. Hydrocortisone administration two hours before the experiment resulted in a negative value of the average deviation, attesting to a significant acceleration of extinction. The development of extinction inhibition was concluded to depend upon the degree and duration of the enhancement of hydrocortisone hormone content in the organism. 14 references. (Journal abstract modified)

219328 Teten'chuk, E. V.; Mekhova, G. M.; Vikulina, N. S.; Gilev, A. P. Laboratoriya farmakologii Nauchno-issledovatel'skogo khimiko-farmatsevticheskogo instituta, Novokuznetsk, U.S.S.R. **/The role of the amygdala in the depressive action of serotonin and 5-hydroxytryptophan on the conditioned activity of white rats./** Rol' mindalevidnogo kompleksa v ugnetayushchem deystvii serotonina i 5-oksitriptofana na uslovnoreflek tornuyu deyatel'nost' belykh krys. Zhurnal vysshey nervnoy deyatel'nosti imeni I. P. Pavlova (Moskva). 24(6):1227-1232, 1974.

The role of the amygdala in the depressive action of serotonin and 5-hydroxytryptophan on the elaboration of a conditioned avoidance reaction was investigated in 12 white rats. Injections of 5-hydroxytryptophan in doses of 150mg/kg were found to lower the amplitude of elicited potentials of the basolateral and central amygdala neurons. Serotonin injections in doses of 25mg/kg elicited a depression of the conditioned avoidance reaction. Bilateral destruction of the amygdala complex neurons and the ventral hippocampus did not effect the ability of 5-hydroxytryptophan to depress the conditioned avoidance reaction. 22 references. (Journal abstract modified)

219332 Avakyan, R. M.; Arshanyan, E. B. Kafedra farmakologii Meditsinskogo instituta, Chita, U.S.S.R. **/The effect of catecholaminergic drugs on the behavior and EEG of rats during corasol seizures./** Vliyaniye katekholaminergicheskikh veshchestv na provedeniye i EEG pri korazolvykh sudorogakh u krys. Zhurnal vysshey nervnoy deyatel'nosti imeni I. P. Pavloa (Moskva). 24(6):1263-1269, 1974.

The effect of catecholaminergic drugs on the behavior and EEG of the cortex, neostriatum, hippocampus and midbrain reticular formation were investigated in rats during corasol seizures. The stimulating catecholaminegic drugs were found to disturb the formation of the preseizure state: the latent period of slow negative EEG waves was prolonged; the manifestation threshold of myoclonic jerks was higher, and their number, smaller. The depressing catecholaminergic drugs were found to facilitate the development of behavioral and EEG predecessors of seizures. The threshold of the first changed significantly only after chlorpromazine and alpha-methyl-DOPA administration. Seizure activity appeared sooner in the neostriatum during chlorpromazine and haloperidol action, and later under the action of the stimulating drugs. The noradrenergic mechanisms of the brainstem reticular formation and the dopaminergic mechanisms of the neostriatum were concluded to play an important role in the development of corasol seizures. 15 references. (Journal abstract modified)

219472 Miyabo, Susumu; Hisada, Tomoichiro; Kishida, Shigeru. Third Department of Internal Medicine, Kanazawa Univ. School of Medicine, Taka-ra-machi 13-1, Kanazawa City, 920 Japan **Studies on behavioral endocrinology of corticosteroids.** Journal of Japanese Psychosomatic Society (Fukuoka). 15(1):40-45, 1975.

The psychoneuroendocrine relationship was investigated in two animal experiments. Results indicate that adrenal steroids influence the rat's emotional behaviors and that such behavioral effects can be separated from the peripheral metabolic effects as glucocorticoid. Neonatal corticosteroid administration had definite effects on the ontogeny of diurnal rhythms of locomotor activity and of plasma corticosterone. There were some critical periods, probably related to the functional maturation of brain, for the psychophysiological effects of adrenal steroids. 19 references. (Journal abstract modified)

219502 Solomatina, E. S.; Klygul', T. A. Laboratoriya eksperimental'noy kardiologii, Instituta normal'noy i patologicheskoy fiziologii AMN SSSR, Moscow **/The effect of diazepam on the behavior of rats adapted to high altutude hypoxia in conflicting situations./** Vliyaniye diazepama na povedeniye adaptirovannykh k vysotnoy gipoksii krys v usloviyakh konfliktnoy situatsii. Farmakologiya i toksikologiya (Moskva). 38(1):20-23, 1975.

The effect of diazepam on the behavior of animals during conflict situations was investigated in normal rats and in those adapted to high altitude hypoxia. A conflict situation was induced by exposing rats to an electric shock when they were drinking, thus simultaneously activating opposing reflexes for drinking and for defense. In a primary conflict situation, diazepam and a long-term adaptation to high altitude hypoxia both tended to eliminate the conflict behavior of rats. In a secondary conflict situation, diazepam barred conflict behavior, whereas adaptation to hypoxia was found to contribute to intensification of the conflict. Introduction of diazepam to animals already adapted to hypoxia strengthened conflict behavior in both primary and repeated conflict situations. 14 references. (Journal abstract modified)

219745 Ayvazashvili, I. M.; Iordanishvili, G. S. Akademiya nauk Gruzinskoy SSR, Institut fiziologii, Tbilisi, U.S.S.R. **/The effect of transamine on psychonervous and conditioned memory in rats./** Vliyaniye transamina na psikhonervnuyu i uslovnoreflektornuyu pamyat' u krys. Soobshcheniya akademii nauk gruzinskoy SSR (Tbilisi). 77(3):701-703, 1975.

The effect of intraperitoneal administration of transamine was investigated on the psychoneural and conditioned memory in rats. Psychoneural memory was manifested by an electrically stimulated emotional reaction of fear. A conditioned stimulus of jumping across a barrier was elaborated in response to both auditory visual stimuli. Transamine administration temporarily inhibits both psychonervous and conditioned memory in rats. The inhibition of memory was tentatively concluded to be due to the inhibitory effect of transamine on monoaminoxidase. 9 references. (Journal abstract modified)

219748 Burov, Yu. V.; Borisenko, S. A. Laboratoriya farmakoterapii ekstermal'nykh sostoyanii, Moscow **/The effect of psychotropic agents on the mental and physical working capacity in rats./** Vliyaniye psikhotropnykh veshchestv na psikhicheskiyu i fizicheskuyu rabotosposobnost' u krys. Byulleten' eksperimental'noy biologii i meditsiny (Moskva). 79(2):45-48, 1975.

The effect of psychotropic substances on tne duration of forced swimming and the speed of learning to find the path through a maze was investigated in 210 white rats. Substances facilitating the self-stimulation reaction (i.e. cocaine, caffeine, morphine, benactyzine, phenobarbital, meprobamate, diazepam, chlordiazepoxide) and substances stimulating the positive brain reinforcement, were found to accelerate the elaboration of the maze learning. Cocaine, morphine, benactyzine, phenobarbital and electrical stimulation of the systems of positive reinforcement increased the duration of forced swimming. Meprobamate, diazepam, and chlordiazepoxide failed to influence swimming duration. It was concluded that the capacity of psychotropic substances to activate the systems of positive reinforcement determines their effect on the physical and mental working capacity of rats. 20 references. (Journal abstract modified)

220473 Jerussi, Thomas P. City University of New York **Pharmacologically induced behavioral correlates of nigrostriatal function. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-9060 HC$13.50 MF$5.00 149 p.

Normal unoperated rats were tested for rotation (circling behavior) in a spherical rotometer and dose response relationships were assessed using d-amphetamine, apomorphine, L-DOPA, haloperidol, and scopolamine. Results suggest that normal rats may have a bilateral asymmetrical content of striatal dopamine, as well as an asymmetrical complement of striatal dopamine receptors. The importance of a nigrostriatal asymmetry was most evident after unilateral lesions of the caudate nucleus, for rats rotated more postoperatively if the lesion was made ipsilateral, rather than contralateral to the S's preoperative direction of rotation. Dopaminergic - cholinergic interactions were evident. Bilateral regional neurochemistry was performed on Ss injected with various doses of d-amphetamine and tested for rotation. The only chemical measure of significance were differences in striatal dopamine content, ipsilateral and contralateral to the direction of rotation induced by the drug. It appears that the neurochemical substrate for rotation in normal rats is the difference in striatal dopamine content. Theoretical implications of results are discussed in relation to arousal, spatial behavior, and handedness, and how these functions could have evolved from the same bilateral striatal asymmetry. (Journal abstract modified)

220474 McCoy, Daniel Joseph, Sr. Indiana University **The combined effects of cannabidiol and delta-9-tetrahydrocannabinol. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-9024 HC$13.50 MF$5.00 152 p.

The combined effects of cannabidiol (CBD) and delta9-tetrahydrocannabinol (EHC) on mice were evaluated, and the results of this combination were characterized. Pretreatment with THC extended both hexobarbital and ethanol induced sleep. CBD gave an even greater extension with hexobarbital, but no effect with ethanol. The combination of THC and CBD produced an effect suggesting a synergistic response. The effects of the two cannabinoids and their mixture on mice receiving stimulant drugs was also investigated. THC depressed spontaneous locomotor activity for the first 60 min of a 4 hour period and caused a biphasic response on methamphetamine induced locomotor activity. From 90 to 150 min, however, activity was increased. CBD altered neither spontaneous nor methamphetamine induced activity when given alone, nor did it change the effects of THC in the mixture. Overall results suggest that CBD and THC are both active pharmacological agents. Both have the ability to alter the effects of the other cannabinoid in an unpredictable manner. This supports the hypothesis that CBD plays a role in the biological activity of marihuana and suggests that CBD, as well as THC, should be considered in evaluation of the potency of a cannabis sample. (Journal abstract modified)

220644 Crabtree, J. Michael. Carnegie-Mellon University **Schedule-induced aggression in laboratory rats: demonstration and control through sodium amobarbital. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-9081 HC$13.50 MF$5.00 63 p.

Two experiments investigated schedule induced aggression in laboratory rats and its demonstration and control through administration of three concentrations of amobarbital sodium. Experiment one attempted to induce the aggression under three conditions: 1) response group, trained to respond in an operant chamber on a fixed-ratio 5 (FR5) schedule of reinforcement; 2) free food group, placement in the operant chamber and receiving response independent food at a rate about equal to that earned by the response group; and no food group, placement in the chamber but not receiving food there. Results indicate a significant increase in most aggressive behaviors during the extinction phase for Ss in the repsonse and free food groups, but not in the no food group. Dominant behavior patterns for the two groups increased, and subordinate behavior patterns increased in stimulus animals. Aggressive behavor returned to its previously low level when food reinforcement was once again made available. The three concentrations of amobarbital sodium (10mg/kg, 20mg/kg, and 30mg/kg) reduced aggressive behaviors during extinction in a linear dose dependent manner. Control data indicate that the reduction was not due to nonspecific effects of the drug. (Journal abstract modified)

220674 Lenard, Lane Gary. Rutgers University **6-Hydroxydopamine and avoidance: a behavioral and pharmacological analysis. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-8411 HC$13.50 MF$5.00 177 p.

The effects of intraventricular administration of 6-hydroxydopamine (6-HD) on the avoidance behavior of rats pretreated with pargyline were examined. The drug caused severe, long-term decreases in avoidance responding, but had little or no effect on escape responding. Despite the fact that the rats failed to avoid, they appeared able to discriminate the conditioned stimulus (CS), which was evident from freezing behavior and other symptoms of an apparent fear reaction during the CS. The increase in freezing, a response which was incompatible with avoidance, was seen during the first test sessions after 6-HD treatment and seemed largely responsible for a gradual decline in avoidance responding during this same period. All data suggest that the two processes proposed to be involved in the appearance of avoidance deficits after 6-HD treatment might be related to separate catecholamine systems in the brain. The learned avoidance behavior seems most closely related with dopamine neurons, while the learned suppression and possible hyperreaction to stress seems a function of activity in norepinephrine neurons. (Journal abstract modified)

220681 Burns, Thomas Crawford. University of Georgia **Investigations of UCS-CS mediation in radiation-induced conditioned taste aversion. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-8101 HC$13.50 MF$5.00 70 p.

The effects of procaine and dimenhydrinate effects on radiation induced taste aversion learning were examined in groups of eight male Sprague-Dawley rats. Neither the local anesthetic procaine, administered intraperitoneally, nor the antinausea drug, dimenhydrinate, administered intramuscularly, blocked acquisition of aversion to saccharin flavored water. Control Ss confirmed that saccharin preferences appeared normally in nonirradiated Ss, and that the drugs produced no aversion in the presence of radiation. Another investigation, using groups of five female Sprague-Dawley rats showed a failure of dimenhydrinate in blocking acquisition of a rotation induced conditioned taste aversion. Two dose levels were used: 1/mg/kg and 2mg/kg. At the dimenhydrinate dosage involving radition (1.75mg/kg) and at the higher dosage used in the rotation examination, a potentiation of the effects of radiation and rotation occurred respectively. Results favor a model for unconditioned stimulus - conditioned, stimulus (UCSH - CS) mediation as being diffuse and perhaps redundant. The possibility that nausea producing stimuli may work synergistically is also discussed. (Journal abstract modified)

220687 Russell, Richard L., Jr. McGill University **Determinants of amphetamine-produced stereotyped behavior in the rat. (Ph.D. dissertation).** Dissertation Abstracts International. Ottawa, National Library of Canada.

Six experiments with rats investigated whether stereotyped behavior produced by amphetamine injection (AMP-SB) is influenced by factors known to affect the stereotypes of mentally retarded and mentally ill persons. Three experiments demonstrated that the incidence of stereotyped behavior is a monotonic increasing function of amphetamine dose. The interpretation of the findings emphasized the importance of the Ss' arousal levels in determining stereotyped behavior. Two studies examined the relationship between environmental novelty and AMP-SB. AMP-SB was lower among Ss placed into novel environments than among Ss placed into familiar environments. The ability of novel stimuli to evoke exploratory responses incompatible with stereotypy is suggested as the basis for this effect. This interpretation was supported in a final experiment, which observed exploratory behavior and general activity, as well as AMP-SB, in Ss exposed to a novel stimulus in an otherwise familiar environment. All six experiments support a unified conception of amphetamine produced and pathological stereotyped behaviors. (Journal abstract modified)

220903 Oka, Makoto; Shimizu, Masanao. Department of Pharmacology, Research Laboratories, Dainippon Pharmaceutical Co. Ltd., Suita-shi, Osaka, Japan **A simple avoidance procedure for testing psychotropic drugs in mice.** Japanese Journal of Pharmacology (Kyoto). 25(2):121-127, 1975.

A simple avoidance procedure in mice was investigated for the purpose of testing psychotropic drugs. A box with two compartments, darkened and lightened, was used. Mice were put into the darkened compartment where they would be punished unless they moved into the lightened compartment within 5 sec. Most mice quickly acquired an active avoidance in this apparatus with training less than 50 successive trials. Major tranquilizers such as chlorpromazine, haloperidol, clozapine and oxypertine depressed the avoidance response at doses lower than those at which the escape response was impaired. Diazepam and doxepin had depressant effects at doses which impaired the escape response. Imipramine and nortriptyline did not affect the avoidance response at the doses tested. It is concluded that mice quickly acquire an active avoidance under the present procedure and that this conditioned behavior is selectively depressed by major tranquilizers. 21 references. (Author abstract)

220946 LeMoal, Michel; Galey, Daniel; Cardo, Bernard. Laboratoire de Psychophysiologie, Institut de Biologie Anamile, Universite de Bordeaux 1, 33405 Talence, France **Behavioral effects of local injection of 6-hydroxydopamine in the medial ventral tegmentum in the rat. Possible role of the mesolimbic dopaminergic system.** Brain Research (Amsterdam). 88(1):190-194, 1975.

The behavioral effects of local injection of 6-hydroxydopamine (6-OH-DA) in the medial ventral tegmentum (VMT) in the rat were examined in terms of the role of the mesolimbic dopaminergic system. Passive avoidance performance was measured 30-45 days after intra-VMT injection in ten 6-OH-DA-treated rats and 8 control animals. The 6-OH-DA treated rats stepped down from the platform significantly sooner than the controls. The results show that the performance of the passive avoidance task in the 6-OH-DA group was inferior to the control group. In order to test the role of the noradrenergic ventral bundle 6-OH-DA was injected bilaterally in this bundle at pons level. After 6-OH-DA injection in ventral noradrenergic bundles, behavior seemed normal in all apparent respects and there was no increase in locomotor activity. It was concluded that selective destruction of the aminergic neurons in the VMT leads to locomotor hyperactivity and a passive avoidance deficit in rats. 15 references.

221005 Squire, L. R.; Emanuel, C. A.; Davis, H. P.; Deutsch, J. A. Dept. of Psychiatry, VA Hospital, San Diego, CA 02161 **Inhibitors of cerebral protein synthesis: dissociation of aversive and amnesic effects.** Behavioral Biology. 14(3):335-341, 1975.

In a study of inhibitors of cerebral protein synthesis, dissociation of aversive and amnesic effects was examined in mice. The results indicate that amnesic doses of cycloheximide and anisomycin, two protein synthesis inhibitors, produced conditioned gustatory aversion. Lithium chloride produced as much conditioned aversion as an amnesic dose of anisomycin and more aversion than cycloheximide, but did not affect memory. Therefore the aversive effect of protein synthesis in-

hibitors, as measured by the conditioned gustatory aversion test, is not sufficient to explain their amnesic effect. 16 references. (Author abstract modified)

221010 Luttge, William G. Dept. of Neuroscience, University of Florida College of Medicine, Gainesville, FL 32610 **Stimulation of estrogen induced copulatory behavior in castrate male rats with the serotonin biosynthesis inhibitor p-chlorophenylalanine.** Behavioral Biology. 14(3):373-378, 1975.

The stimulation of estrogen induced copulatory behavior in castrate male rats with the serotonin biosynthesis inhibitor p-chlorophenylaladine (PCPA) is reported. Treatment with PCPA in combination with suboptimal injections of estradiol benzoate resulted in a dramatic facilitation in the display of male sexual behavior. Mount and intromission frequency were found to increase, while latency to the first mount and intromission were found to decrease following PCPA treatment. Ejaculatory behavior was also found to be stimulated by PCPA. Results are discussed in terms of the aromatization and serotonin theories of the control of male sexual behavior in the rat. 21 references. (Author abstract)

221039 Koob, George F.; Spector, N. H.; Meyerhoff, J. L. Dept. of Neurophysiology, Walter Reed Army Institute for Research Washington, DC 20012 **Effects of heroin on lever pressing for intracranial self-stimulation, food and water in the rat.** Psychopharmacologia (Berlin). 42(3):231-234, 1975.

The effects of heroin on lever pressing for intracranial self-stimulation (ICSS), food and water were examined in the rat. Male rats maintained with continuous access to levers for ICSS, water, and food were subjected to five consecutive daily injections of heroin. Rates of lever pressing for ICSS were increased in eight rats, 2 to 6 hrs after administration of heroin. Rates of lever pressing for water and food were not significantly changed during this period. Naloxone (5mg/kg) pretreatment attenuated by 82% the facilitative effect of heroin on ICSS. A second group of 8 rats maintained at reduced ICSS rates failed to show an increase in lever pressing for ICSS with heroin. Results are consistent with previously reported studies describing the effects of morphine on ICSS. 8 references. (Author abstract modified)

221040 Castellano, Claudio. Labortorio de Psicobiologia e Psicofarmacologia, C.N.R., Rome **Effects of morphine and heroin on discrimination learning and consolidation in mice.** Psychopharmacologia (Berlin). 42(3):235-242, 1975.

The effects of morphine and heroin on discrimination learning and consolidation in mice were examined. Morphine and heroin were administered to mice learning to swim toward a light source (L procedure) or toward the dark (D procedure), in a Y water maze, under pre trial and posttrial drug treatment conditions. In the pretrial experiments a clear disrupting effect on performance with the two procedures followed administration of both drugs, but for the L procedure, performance never fell below the 50% level of correct choices. Analysis of the performance within each session demonstrated a disruption in the long-term memory consolidation mechanism. The administration of naloxone, or alternatively, discontinuation of the treatment, was followed by a gradual improvement, in performance by the treated animals. In both procedures, a performance disruption also followed the administration of the drugs immediately after each experimental session. 20 references. (Author abstract)

221041 Furukawa, Tatsuo; Ushizima, Itsuko; Ono, Nobufumi. Department of Pharmacology, School of Medicine, Fukuoka University, Fukuoka, Japan **Modifications by lithium of behavioral responses to methamphetamine and tetrabenazine.** Psychopharmacologia (Berlin). 42(3):243-248, 1975.

The modification by lithium of behavioral responses to methamphetamine and tetrabenazine are reported. Different groups of mice were injected s.c. daily with lithium chloride in three doses or with saline for a period of 3 weeks. Lithium administered acutely or chronically did not affect spontaneous locomotor activities. However, methamphetamine induced hyperlocomotor activities were inhibited in the lithium groups as compared with those in the saline group, while the hyperlocomotor activities induced by tetrabenazine in the nialamide pretreated animals were reduced to some extent but not significantly by lithium. Tetrabenazine brought about an initial transient increase followed by a decrease of spontaneous locomotor activities in the lithium groups, whereas it induced only a decrease of the activities in the saline group. These effects of lithium tended to increase with an increase of the doses administered and with a prolongation of its daily administration. The results demonstrate that lithium modifies behavioral responses to methamphetamine and tetrabenazine. 37 references. (Author abstract modified)

221043 Miczek, Klaus A.; Lau, Peter. Department of Psychology, Carnegie-Mellon University, Pittsburgh, PA 15213 **Effects of scopolamine, physostigmine and chlordiazepoxide on punished and extinguished water consumption in rats.** Psychopharmacologia (Berlin). 42(3):263-269, 1975.

The effects of scopolamine, physostigmine and chlordiazepoxide on punished and extinguished water consumption were studied in rats. Scopolamine hydrobromide, a centrally and peripherally acting antimuscarinic agent and physostigmine sulfate, a centrally and peripherally acting acetylcholinesterase inhibitor, lowered both nonpunished and punishment suppressed water intake and lick rate, whereas their quaternary analogs which primarily act in the periphery, had no significant effect at comparable dose levels. Scopolamine and physostigmine suppressed punished water consumption at lower dose levels than nonpunished intake. Chlordiazepoxide enhanced punished as well as nonpunished water intake. In a further experiment comparing punishment and extinction suppression, scopolamine and physostigmine did not affect punished or extinguished water intake; chlordiazepoxide reliably increased punished, but not extinguished licking on the water nozzle. These results suggest that scopolamine and chlordiazepoxide do not act via a common mechanism, and that punishment and extinction suppression are not a pharmacological entity. 31 references. (Author abstract modified)

221047 Hughes, R. N.; Greig, Andrea M. Department of Psychology, University of Canterbury, Canterbury, Christchurch, 4, New Zealand **Chlordiazepoxide effects on reactions to novelty and activity with and without prior drug experience.** Psychopharmacologia (Berlin). 42(3):289-292, 1975.

Reactions to novelty, rearing and ambulation were observed in rats following saline or chlordiazepoxide injections either with or without prior drug experience. Drug suppression of the former two responses was evident but there was no indication of prior drug experience being effective. However, experience appeared to negate the compound's depressant effect on ambulation shown by inexperienced subjects. It was concluded that inhibitory influences of chlordiazepoxide on reactions to novelty and rearing can not be ascribed to the aversive effects of a novel drug state. 18 references. (Author abstract)

221048 Buckett, W. R.; Shaw, J. S. Pharmacological Dept., NOVO Terapeutisk Laboratorium A/S NOVO Alle, DK-2880, Bagsvaerd, Copenhagen **Dopaminergic drugs antagonized the psychotomimetic effects of partial-agonist analgesics.** Psychopharmacologia (Berlin). 42(3):293-297, 1975.

The psychotomimetic actions of the partial agonist analgesic drugs cyclazocine and levallophan were demonstrated using a quantitative behavioral test in young rats which measures lateral head movements and pivoting on the hind paws. This drug induced behavior was antagonized by low doses of the dopaminergic agonists apomorphine and piribedil, the dopamine releasing drug amphetamine, the dopamine reuptake blocking agent benztropine and by large doses of the dopamine precursor L-Dopa. Naloxone antagonized the behavior, but only at 100 times the analgesic antagonist dose. These results show that dopaminergic systems are implicated in the mechanism of action of partial agonist induced psychotomimetic side-effects. 24 references. (Author abstract)

221049 Saucier, D.; Astic, L. Laboratoire de Physiologie Neuro-Sensorielle, Universite Claude Bernard, Lyon I, Villeurbanne, France **/Effects of alpha-methyl-dopa on newborn kitten sleep. Behavioral evolution during the first month after-birth./** Effects de l'alpha-methyl-Dopa sur le sommeil du chat nouveau-ne. Evolution comportementale au cours du 1er mois post-natal. Psychopharmacologia (Berlin). 42(3):299-303, 1975.

The paradoxical sleep (PS) suppressing effect of alpha-methyl-dopa was studied in kittens at birth. The newborn animal received daily injections of alpha-methyl-dopa during the first 2 weeks of life. States of sleep were studied during the treatment (days 1 to 14) and after administration of the drug halted (days 15 and 16). Daily injections of alpha-methyl-dopa induced an average PS deprivation of 72%. This deprivation was compensated for by a significant increase in quiet sleep (QS) rate which was found to be up to 3.5times that of kittens not receiving alpha-methyl-dopa. A progressive return of PS ratio to normal, without PS rebound, was observed after drug administration ceased. Alpha-methyl-dopa produced a sedative effect on the kitten which remained relatively hypotonic during the treatment. Behavioral studies carried out over the first month after birth showed no significant delay in the ponderal growth nor in the acquisition of stereotyped behavior patterns. However motor coordination was delayed 2 weeks in the kittens. 11 references. (Author abstract)

221052 Bovet-Nitti, Filomena; Messeri, Patrizia. Laboratorio di Psicobiologia e Psicofarmacologia, C.N.R. 1, via Reno - 00198 Rome **Central stimulating agents and population growth in mice.** Life Sciences (Oxford). 16(9):1393-1402, 1975.

The relationship between central stimulating agents and population growth was examined in mice. Population growth curves of random bred mice confined in 18 dm2 cages show, after a steep increase, a period of numerical equilibrium from about the 12th week, with an average density of 400 animals m2. After this period, a progressive decrease is observed, until all the animals die after 700-1000 days. Chronic administration of caffeine and amphetamine induces a block of the population growth; different components of aggressiveness can be identified as responsible. On the contrary, high doses of nicotine do not affect either the population growth or its structure. 18 references. (Author abstract)

221340 Sassenrath, E. N.; Chapman, L. F. University of California School of Medicine, Davis, CA 95616 **Tetrahydrocannabinol-induced manifestations of the "marihuana syndrome" in group-living macaques.** Federation Proceedings. 34(8):1666-1670, 1975.

The effects of long-term frequent use of marihuana on behavior and neuroendocrine function was examined in monkeys. For a year, young adult macaques were given 2.4mg/kg tetrahydrocannabinol (THC) daily, a dose equivalent to a daily intake of .4mg/kg of THC by smoking in man. The results to date have confirmed the absence of pronounced behavioral or endocrine derangements in the long-term THC exposed subjects. Recognition by cagemates of the altered social responsiveness of drugged subjects was a sensitive index of drug effects. Changes in affiliative behaviors reflect sedative effects of THC, as active social interaction (playing) was replaced by passive affiliative behavior (huddling with preferred cagemates). A consistent, persistent change in affect or "personality" was manifested in a social context as increased irritable aggressiveness after the development of behavioral tolerance to the initial effects of THC. There was no evidence of testosterone depression in males, derangement of menstrual cycles, conception, or lactation in females, or of changes in stress response systems. 7 references.

221766 Houser, Vincent P. Psychotropic Drug Laboratory, Veterans Administration Hospital, Perry Point, MD **Effects of ACTH, dexamethasone and deoxycorticosterone on aversive threshold of rats.** Psychological Reports. 36(3):787-792, 1975.

The effects of adrenocorticotropic hormone (ACTH), dexamethasone and deoxycorticosterone upon the aversive threhold of the rat were investigated using the spatial preference technique. Both ACTH and dexamethasone reduced the mean aversive threshold during the initial presentation of the compound, but only dexamethasone produced decrements that were statistically reliable. Subsequent administration of these two substances produced no reliable effects upon the aversive thershold. Various doses of deoxycorticosterone produced no consistent changes in the threshold to electric shock. None of the substances were able to reliably alter motor activity on this test. It is concluded that these acute changes in adrenocortical activity have little prolonged effect upon the aversive threshold to grid shock in the rat. 16 references. (Author abstract)

221799 Houser, Vincent P.; Rothfeld, Benjamin; Varady, Alexander, Jr. Psychotropic Drug Laboratory, Veterans Administration Hospital, Perry Point, MD 21902 **Effects of chlordiazepoxide upon fear-motivated behavior in dogs.** Psychological Reports. 36(3):987-998, 1975.

The effects of several doses of chlordiazepoxide upon the behavioral and physiological reactions displayed when dogs were subjected to a Sidman nondiscriminated avoidance schedule which contained seven conditioned stimuli (CS) - unavoidable shock (US) pairings were studied. The drug reliably reduced baseline response rate and significantly inhibited the amount of urinary cortisol excreted during the experimental sessions. Facilitation of heart, response, and activity rates normally noted during the aversive CS were unaffected by administration of the drug. In addition, overall heart-rate showed no consistent pattern of results in response to drug administration. It is concluded that under this schedule of reinforcement, only the baseline response rate and urinary cortisol measures are sensitive to the antianxiety effects of chlordiazepoxide. 21 references. (Author abstract)

222090 Edmonds, Don Erwin. University of Pennsylvania **The effect of alpha-methyl-p-tyrosine methyl ester on temporal summation in the neural substrate for the reinforcement effect in self-stimulation. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-14560 HC$13.50 MF$5.00 143 p.

An aspect of self-stimulation behavior in a runway which reflects the amount of reward excitation produced by brain stimulation of the rat was investigated. This measure is shown to be independent of various performance variables, including magnitude of the drive like aftereffect of electrical stimulation of the brain (ESB), state of health, task difficulty, pharmacological debilitation, and athletic skill. Specifically, the hypothesis that the synaptic release of catecholamines is responsible for the reward effect of brain stimulation was tested. Rats were treated with the catecholamine synthesis inhibitor alpha-methyl-p-tyrosine methyl ester (AMPT) and subsequently injected with L-dopa and a peripheral decarboxylase inhibitor. Results show that brain stimulation reward is not homogenous. For some electrodes, AMPT dramatically depressed performance for brain stimulation reward without altering the reward effect of the ESB. For others, the rewarding property of the ESB was reduced or abolished by AMPT and was restored by L-dopa. These two effects can occur on two different electrodes in the same rat, suggesting that some, but not all, reward neurons release catecholamines. (Journal abstract modified)

222114 Wood, Ronald Wesley. Univeristy of Rochester **The effects of shock intensity, d-amphetamine, and pento-barbital on the frequency and response dynamics of biting attack in the squirrel monkey. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-15235 HC$13.50 MF$5.00 85 p.

The effects of shock intensity, d-amphetamine, and pentobarbital on the frequency and response dynamics of biting attack were examined in the squirrel monkey to determine the propensity to bite inanimate objects under such conditions. Most of the Ss displayed biting that was not confined to the period immediately after shock. The behavior of one S suggests that biting immediately after shock is of greater intensity and duration than bites distributed throughout the intershock interval. Biting attack is a multiply determined process which bears no simple relationship to drug dosage. Moderate doses of d-amphetamine produced further increases of high biting attack rates, whereas moderate doses of sodium pentobarbital did not. Furthermore, the frequency, intensity and duration of biting attack episodes can display differential sensitivity to pharmacologic insult, suggesting new dimensions along which drugs of potential or demonstrated clinical utility could be evaluated. (Journal abstract modified)

222263 Everitt, B. J.; Fuxe, K.; Hokfelt, T.; Jonsson, G. Department of Anatomy, University of Cambridge, Downing Street, Cambridge CB2 3DY, England **Role of monoamines in the control by hormones of sexual receptivity in the female rat.** Journal of Comparative and Physiological Psychology. 89(6):556-572, 1975.

The involvement of indoleamines and catecholamines in the hormonal regulation of sexual receptivity was investigated in ovariectomized female rats. Drugs that reduce 5-hydroxytryptamine, dopamine, and adrenaline or increase noradrenaline neurotransmission tended to facilitate the occurrence of estrous behavior in estrogen treated females, and drugs having opposite effects tended to inhibit receptivity induced by estrogen and progesterone. Estrogen decreased noradrenaline turnover in cortex and brainstem; progesterone enhanced this effect in brainstem but prevented it in cortex. Both hormones tended to block noradrenaline uptake in hypothalamus in vitro. In a schedule used to induce receptivity, estrogen accelerated serotonin turnover, an effect prevented by progesterone. It is concluded that a number of monoamines are involved in the control by hormones of estrous behavior. Furthermore, hormones affect both amine turnover and uptake mechanisms. 85 references. (Author abstract)

222265 Price, Marion T. C.; Cooper, R. M. Department of Psychiatry, Kinsmen Laboratory of Neurological Research, University of British Columbia, Vancouver 8, B.C., Canada **U-shaped functions in a shock-escape task.** Journal of Comparative and Physiological Psychology. 89(6):600-606, 1975.

The hypothesis was tested that the U-shaped retraining curve in rats trained on a light going shock - escape task reflects fluctuations in the strength of memory for the light going habit. In experiment one, rats given limited training on a light discrimination shock - escape task (Phase 1) were divided into groups and retrained to criterion (Phase 2) from 30 min to 17 days later. A U-shaped retraining curve was obtained with best performance at 3 and 5 days. U-shaped curves were also found in experiments two through four, when the light cue was reversed for Phase 2 and when shock alone or an injection of epinephrine was given in lieu of Phase 1 training. In experiment five, an injection of physostigmine was found to improve maze performance. It is concluded that the low point of the U-shaped curve reflects a rebound period of parasympathetic dominance following a period of high sympathetic activity associated with the stress of painful shocks. The hypothesis was not confirmed. 21 references. (Author abstract modified)

222268 James, David T. D. School of Biological and Environmental Studies, New University of Ulster, Coleraine, County Londonderry, Northern Ireland **Posttrial d-amphetamine sulfate and one-trial learning in mice.** Journal of Comparative and Physiological Psychology. 89(6):626-635, 1975.

Experiments are reported which show that 2mg/kg of d-amphetamine sulfate injected intravenously immediately after footshock on a one trial passive avoidance learning task impairs the performance of mice in retention tests 24 hr and 96 hr later. When the injection was delayed by as little as 90 sec, no such impairment was seen. A similar intravenous injection immediately after the learning trial of a water rewarded one trial appetitive task had no discernible effect on performance in retention trials 24 hr and 6 wk later. It is argued that the effects of the amphetamines on learning behavior depend on whether reward or punishment is involved and, further, that all such effects can be accounted for in terms of the drugs' influence on memory mechanisms. 28 references. (Author abstract)

222638 Chance, William Terry. Northern Illinois University **Central nervous system pharmacology of cholinergically elicited eating and drinking behavior in the albino rat. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-13155 HC$13.50 MF$5.00 157 p.

The question of whether intrahypothalamic injections of solutions of carbachol would elicit eating and tested the proposed model of cholinergic-adrenergic interaction was examined in the rat. In the first two experiments injections of carbachol were tested across five stimulations for elicitation of eating and drinking. The third experiment investigated the effects of pretreatments with equimolar doses of a nicotinic cholinergic antagonist (hexamethonium) and a muscarinic cholinergic antagonist (atropine) on eating and drinking elicited by subsequent carbachol stimulations. The fourth experiment tested the effects of pretreatments with an alpha-adrenergic antagonist (phentolamine) and a beta adrenergic antagonist (propranolol) on eating and drinking following the injection of

carbachol. In all experiments injections of carbachol were found to elicit significantly more eating and drinking than the control manipulations. Hexamethonium had no significant effect on either behavior. Neither of the adrenergic antagonists (alpha or beta) significantly affected eating or drinking. Since neither cholinergic antagonist effectively reduced eating, it is suggest that this effect may be mediated by a third type of cholinergic receptor. (Journal abstract modified)

222736 Clancy, John Joseph. Wayne State University **The effect of an adrenal demedullation and chemical sympathectomy (2,4,5-trihydroxyphenylethylamine) on the acquisition of a one-way active avoidance response. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-13304 HC$13.50 MF$5.00 193 p.

The effects of adrenal demedullation and a simultaneous central and peripheral 6-hydroxy-dopamine (6-OHDA) lesion on acquisition in an emotional learning situation were examined in rats. In a comparison between the control and demedullation Ss there was no significant difference in rate of acquisition of the avoidance response on both the measures of response latency and number of avoidance responses. Both the control and demedullated Ss learned the escape and avoidance behavior equally well. A norepinephrine fluorescence assay determined that 6-OHDA injections greatly depleted norepinephrine levels in both the central and peripheral nervous systems. The results that a chemical adrenergic lesion has a detrimental effect on both escape and avoidance learning and a total inhibitory effect on avoidance learning were supported by previous findings in the 6-OHDA adrenergic lesion literature. These results support two basic premises of the peripheral physiologic theory of emotional learning: that the adrenergic system is necessary for emotional learning, and that a two factor process is involved in emotional learning. (Journal abstract modified)

222739 Henrik, Elizabeth. Tulane University **Facilitatory and inhibitory influences of progesterone, 20alpha-hydroxyprogesterone and methysergide on the receptive behavior of the female rat. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-11897 HC$13.50 MF$5.00 156 p.

The gradual increase or progressive facilitation of receptivity was studied in adult, ovariectomized female rats. The effect of estradiol benzoate (EB), progesterone (P), 20alpha-hydroxyprogesterone (20alpha-OHP), methysergide (Me), and vaginal stimulation was evaluated. Receptivity score (R.S.)and its components: lordosis, holding, and darting were recorded. The highest R.S. occurred with P, followed by Me, 20alpha-OHP, and oil. The rate of increase under EB was greatest with P, and under EB it was the same with all synergists and oil. Lordosis and holding increased with all synergists, darting increased with P and Me. Only lordosis increased with oil. R.S.,lordosis, and darting increased when vaginal masks were applied. Switching of the synergists changed all scores to the level of the new synergist. Switching from oil to P increased all scores to the levels obtained with P. Removal of vaginal masks increased holding. It is concluded that progressive facilitation of receptivity is dependent on the successive injections of EB. Synergists contribute only to the absolute level of receptivity. Vaginal stimulation does not influence progressive facilitation. (Journal abstract modified)

222749 Stripling, Jeffrey Simmons. University of Colorado **Genetic, biochemical, and environmental variables in the expression of short-term memory in the mouse. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-13111 HC$13.50 MF$5.00 163 p.

Endogenous differences in cholinergic functioning, as indexed by enzyme activity levels, were examined in relation to the expression of short-term memory in the mouse. The primary characteristics of short-term memory in the three strains were similar, although strain differences were found at the shortest and longest delay intervals which were examined. In addition, the strains differed significantly in the activity of both enzymes, the DBA strain having the highest activity and the AKR strain the lowest. A circadian rhythm was found to exist in the activity of choline acetyltransferase but not acetylcholinesterase. Scopolamine disrupted short-term memory but physostigmine had no significant effect. It was concluded that short-term memory is sensitive to sensory input and that drugs which alter cholinergic transmission may affect short-term memory by altering sensory processing. (Journal abstract modified)

222801 Yamato, Tsuneyuki; Ueki, Showa. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka, Japan **Behavioral effects of 2,5-dimethoxy-4-methylamphetamine (DOM) in rats and mice.** European Journal of Pharmacology (Amsterdam). 32(2):156-162, 1975.

The characteristics of the behavioral effects of 2,5-dimethoxy-4-methylamphetamine (DOM or STP) were compared with those of mescaline and methamphetamine in rats and mice. DOM significantly increased locomotor activity in an open-field situation, but at doses above 5mg/kg i.p. it caused biphasic changes, i.e. an initial decrease followed by an increase in motility and exploratory behavior. This hyperactivity was not accompanied by simultaneous increase in rearing. DOM induced head twitches in rats as well as in mice at doses above 0.1mg/kg i.p.,and marked backward locomotion only in rats at doses larger than 5mg/kg i.p. The occurrence of backward locomotion might be attributable to the initial decrease in general activity. Behavioral effects of DOM were different from those of either mescaline or methamphetamine, although they resembled those of mescaline in some respects. 18 references. (Author abstract)

222806 Risner, Marc E. National Institute on Drug Abuse, Div. of Research, Addiction Research Center, Lexington, KY **Intravenous self-administration of d- and l-amphetamine by dog.** European Journal of Pharmacology (Amsterdam). 32(2):344-348, 1975.

The relative potency of d-amphetamine and l-amphetamine to maintain i.v. self-administration behavior was studied. Dogs were trained to work for response contingent drug infusions until a stable drug intake per 4 hr daily session was achieved. Then two unit doses of d-amphetamine and three unit doses of l-amphetamine were evaluated in a parallel line bioassay. Each combination of drug and unit dose was examined separately for five consecutive daily sessions. Order of treatment presentation was determined by a Latin square design. By comparing the unit doses of d-amphetamine and l-amphetamine which yielded the same rate of self-administration it was found that 1mg of l-isomer is equivalent to 0.17mg of the d-isomer. 22 references. (Author abstract)

222807 Hamburger-Bar, Rachel; Rigter, Henk. Pharmacology Department, Scientific Development Group, Organon, Oss, The Netherlands **Apomorphine: facilitation of sexual behaviour in female rats.** European Journal of Pharmacology (Amsterdam). 32(2):357-360, 1975.

Sexual receptivity of spayed female rats was studied by recording lordosis responses to a mounting male. Administration of apomorphine to estrogen and progesterone primed females produced an increase in lordosis behavior 2-48 hr after injection. An increase was also found when apomorphine was substituted for progesterone. These results suggest a role for dopamine in controlling sexual receptivity. 13 references. (Author abstract)

222814 Cohn, M. L.; Cohn, M.; Taylor, F. H.; Scattaregia, F. Department of Anesthesiology, Magee-Womens Hospital, Pittsburgh, PA **A direct effect of dibutryl cyclic AMP on the duration of narcosis induced by sedative, hypnotic, tranquiliser and anaesthetic drugs in the rat.** Neuropharmacology (Oxford). 14(7):483-487, 1975.

The ability of exogenously administered N6,O2'-dibutyryl analog of cyclic adenosine monophophate to shorten, in a dose related manner, the duration of narcosis of eight structurally different agents (chloral hydrate, paraldehyde, diazepam, amobarbital, halothane, ketamine, ethanol and methanol) has been demonstrated in the rat. No other nucleotide, neurotransmitter, biogenic amine or hormone tested shortened in a dose related manner the sleeping time induced by the anesthetic agents. 20 references. (Author abstract)

222815 Kulig, Beverly M. Fysiologie Laboratorium, Rijksuniversiteit Leiden, Leiden, The Netherlands **The effects of thyrotropin-releasing hormone on the behaviour of rats pretreated with alpha-methyltyrosine.** Neuropharmacology (Oxford). 14(7):489-492, 1975.

The effects of synthetic thyrotropin releasing hormone (TRH) on spontaneous motor activity and conditioned avoidance behavior were studied in rats following treatment with alpha-methyltyrosine. Motor activity was measured for four groups of rats for 20 min daily for 4 days prior to drug treatment. Twelve hours prior to the fifth session, groups 3 and 4 received three injections of alpha-methyltyrosine spaced 4 hr apart. Twenty minutes prior to testing, one group received TRH and the other, saline. Groups 1 and 2 were given only TRH or saline 20 min prior to the fifth session. Results indicate that there was no difference between TRH treated subjects and saline controls with endogenous levels of norepinephrine intact. However, TRH antagonized the depressant effects of alpha-methyltyrosine on motor activity. In addition, a second experiment demonstrated that TRH also altered the depressant effects of alpha-methyltyrosine on conditioned avoidance behavior. The results are discussed in terms of possible biochemical mechanisms for an interaction between TRH and central catecholaminergic pathways. 14 references. (Author abstract)

222816 Jacobs, B. L; Wise, W. D.; Taylor, K. M. Department of Psychology, Princeton University, Princeton, NJ 08540 **Is there a catecholamine-serotonin interaction in the control of locomotor activity?** Neuropharmacology (Oxford). 14(7):501-506, 1975.

A catecholamine/serotonin interaction in the control of locomotor activity was examined in the rat. The data demonstrate that this increased response to amphetamine was obtained following lesions specific to the median raphe nucleus, whereas lesions of the dorsal raphe nucleus were without effect. The results also question the validity and generality of the catecholamine/serotonin interaction hypothesis by demonstrating: 1) that when the data are plotted as a percent of baseline activity, the interaction disappears; and 2) that a very similar effect is observed when amphetamine injections are replaced by scopolamine injections. 10 references. (Author abstract modified)

222817 Doggett, N. S.; Reno, H.; Spencer, P. S. J. Department of Applied Pharmacology, Welsh School of Pharmacy, UWIST, Cardiff, Wales **Narcotic agonists and antagonists as models for potential antidepressant drugs.** Neuropharmacology (Oxford). 14(7):507-515, 1975.

The effects of (+)-amphetamine, desmethylimipramine and isocarboxazid on spontaneous locomotor activity and body temperature, together with their activity in two laboratory models of depression produced in mice by the injection of reserpine or tetrabenazine, were compared with those of morphine, cyclazocine and naloxone. Whereas cyclazocine exhibited a weak, transient central stimulant effect, there was no marked similarity between the behavioral effects of morphine or naloxone and those of the representative antidepressants. After peripheral administration, both cyclazocine and morphine antagonized the hypothermia, ptosis and behavioral depression induced by reserpine, but naloxone was inactive. Following direct injection into the cerebral ventricles, very small doses of all three agents showed antireserpine activity. Although morphine, cyclazocine and naloxone could reverse previously established hypothermia and behavioral depression induced by tetrabenazine, pretreatment with these agents could not prevent the depressant effects from developing. The pharmacological behavior of morphine, cyclazocine and naloxone, together with the known clinical activity of cyclazocine is so far consistent with the possibility that all three may have some component of clinical antidepressant activity. 27 references. (Author abstract)

222818 Schlosser, W.; Franco, S.; Sigg, E. B. Research Division, Hoffman-La Roche Inc., Nutley, NJ 07110 **Differential attenuation of somatovisceral and viscerosomatic reflexes by diazepam, phenobarbital and diphenylhydantoin.** Neuropharmacology (Oxford). 14(7):525-531, 1975.

The differential attenuation of somatovisceral and viscerosomatic reflexes by diazepam, phenobarbital and diphenylhydantoin was examined in the cat. In the chloralose anesthetized cat, stimulation of forelimb cutaneous afferent nerves evoked a response in the preganglionic splanchnic nerve, consisting of a short duration spinal reflex followed by a supraspinal component of longer duration. Diazepam markedly attenuated the supraspinal reflex but had a considerably lesser effect on the segmental response. Diphenylhydantoin reduced predominantly the spinal component, while the supraspinal reflex was frequently enhanced after the initial dose. This effect of diphenylhydantoin on the spinal reflex was direct, since it also occurred in the spinal cat. Phenobarbital was approximately equally potent in reducing both the spinal and supraspinal reflex. Visceromotor reflexes were markedly depressed by very small doses of diazepam and by larger doses of phenobarbital. The results indicate that the three central nervous system depressants differentially affect the spinal and supraspinal components of the somatosympathetic reflex. 17 references. (Author abstract modified)

222820 De Wied, D.; Witter, A.; Greven, H. M. Rudolf Magnus Institute for Pharmacology, Medical Faculty, University of Utrecht, Vondellaan 6, Utrecht, The Netherlands **Behaviourally active ACTH analogues.** Biochemical Pharmacology (Oxford). 24(16):1463-1468, 1975.

The role of pituitary peptides such as adrenocorticotropic hormone (ACTH) in the formation and maintenance of learned behavior is reviewed. Specific amino acid sequences which

seem to exhibit significant behavioral activity are identified. Studies with vasopressin analog revealed that the effect of these peptides on conditioned avoidance behavior was of a long-term nature, in contrast to that of ACTH analogs which exert a short-term effect. The site of the behavioral action of ACTH analogs is in midbrain limbic structures, as derived from lesion and implantation studies. The mesodiencephalic area and more specifically the nuclei parafascicularis appeared to be essential for the behavioral effect of ACTH analogs. As revealed from biochemical studies, the mechanism of action probably is located in the cell membranes of midbrain limbic structures. Treatment of hypophysectomized rats with ACTH 1-10 enhanced, with 7-D-Phe-ACTH 1-10 impaired, and with ACTH 11-24 did not affect, the incorporation of (3H)leucine into brainstem cytoplasmic protein. The biochemical effects therefore run parallel with the behavioral effects of these three analogs. 39 references.

223013 Mekhedova, A. Ya.; Luk'yanova, S. N. Institut vysshey nervnoy deyatel'nosti i neyrofiziologii AN SSSR, Moscow **/An experimental analysis on the effects of the psychostimulator sydnocarb./** Eksperimental'nyy analiz effektov psikhostimulyatora sidnokarba. Farmakologiya i Toksikologiya (Moskva). 38(3):267-269, 1975.

The effects of sydnocarb on dogs and rabbits was investigated by conditioned reflex elaboration, electrographic and behavioral tests. Sydnocarb was found to initially have a stimulating effect in both rabbits and dogs. In dogs, however, the stimulating effect was replaced by inhibitory action on the day following drug introduction. Sydnocarb also elicited wild fluctuations in heartrate in both dogs and rabbits. Electrographic effects of sydnocarb were intially prominent in the cortical structures of the rabbit's brain, but proved most intensive in the limbic structures when drug dosage was increased. Sydnocarb was concluded to be effective in treating emotional tension. 5 references. (Journal abstract modified)

223033 Gadusek, Frank J.; Kalat, James W. Duke University, Durham, NC 27706 **Effects of scopolamine on retention of taste-aversion learning in rats.** Physiological Psychology. 3(2):130-132, 1975.

The effects of scopolamine on retention of taste aversion learning were investigated in rats poisoned 90 min after drinking a novel sucrose solution. Two or 4 days later, rats were tested for learned aversions to sucrose while under the influence of various doses of scopolamine. In three replications, no substantial effect of scopolamine on retention of learned taste aversions was observed. It is suggested that taste aversion learning may be less dependent on changes in cholinergic synapses than are certain other types of learning. 8 references. (Author abstract)

223039 Hughes, R. N.; Greig, Andrea M. Department of Psychology, University of Canterbury, Christchurch, 1, New Zealand **Spontaneous alternation in ferrets following treatment with scopolamine, chlordiazepoxide, and caffeine.** Physiological Psychology. 3(2):155-156, 1975.

Spontaneous alternation frequencies were observed in ferrets following injections of saline or two doses of scopolamine, chlordiazepoxide or caffeine. All three drugs significantly reduced alternation while having no effect on choice latencies. Results are discussed in the light of their comparative relevance and theories based on central cholinergic activity. 19 references. (Author abstract)

223040 Houser, Vincent P. Psychotropic Drug Laboratory, Veterans Administration Hospital, Perry Point, MD 21902 **The effects of delta9-tetrahydrocannabinol upon fear-motivated behavior in squirrel monkeys.** Physiological Psychology. 3(2):157-161, 1975.

The effects of three doses of delta9-tetrahydrocannabinol (THC) on the behavior of six squirrel monkeys subjected to a Sidman nondiscriminated avoidance schedule that superimposed conditioned stimuli (CS) -- unavoidable shock pairings upon the ongoing avoidance behavior were studied. All Ss demonstrated facilitated avoidance response rates and general motor activity during the aversive CS. Oral administration of THC produced avoidance decrements with a consequent increase in the number of shocks received only under the highest dosage. All doses reduced the facilitation of avoidance response rates normally noted during the aversive CS and severely reduced general motor activity. Results suggest that THC may reduce the level of fear normally generated during presentation of an aversive CS previously associated with unavoidable shock. 18 references. (Author abstract)

223044 Sjoden, Per-Olow; Soderberg, Ulf. Neurophysiological Laboratory, Ulleraker Hospital, University of Uppsala, S-75017, Uppsala, Sweden **Long-lasting effects of prenatal 2,4,5-trichlorophenoxyacetic acid on open-field behavior in rats: pre- and postnatal mediation.** Physiological Psychology. 3(2):175-178, 1975.

A single dose of 2,4,5-trichlorophenoxyacetic acid (2,3,5-T) was given to 12 female rats in the first week of pregnancy to determine its effects on offspring open-field behavior. Controls received oil vehicle. At birth, half of the drug treated and half of the oil treated litters were cross-fostered. Open-field behavior was studied in separate groups of offspring at 35, 50, 95, and 125 days of age. Results at 35 and 60 days showed a prenatal, as well as a postnatal augmenting effect on ambulating and rearing, particularly on the first day of resting. No effects were obtained at 95 days. At 125 days, a postnatal depressing effect of prenatal, 2,4,5-T was suggested for rearing behavior. A possible relationship between the rate of exploratory reactions and the thyroid activity in these Ss is discussed. 13 references. (Author abstract)

223062 Zaostrovskiy, O. V.; Mil'shteyn, G. I. Voyenno-meditsinskaya akademiya im. S. M. Kirova, Leningrad **/The effect of neurotropic agents on motor hyperactivity in dogs induced by amizyl./** Vliyaniye neyrotropnykh sredstv na dvigatel'noye vozbuzhdeniye sobak, vyzvannoye amizilom. Byulleten' eksperimental'noy biologii i meditsiny (Moskva). 79(5):59-61, 1975.

The effect of neurotropic agents on motor activity was investigated in dogs under the influence of amizyl. Motor activity was recorded quantitatively before and after intramuscular injections of amizyl in doses of 2mg/kg. Amizyl induced hyperactivity for 2-3 hours; galanthamine injections blocked the effect of amizyl. Etaperazine was the most active of the neuroleptic tranquilizers tested. Chlorpromazine and diazepam deranged the dogs' state. Diazepam and haloperidol potentiated the effect of amizyl. Motor hyperactivity induced by amizyl was tentatively concluded to involve anticholinergic mechanisms; neuroleptics with cholinolytic properties were therefore concluded to be unsuitable for the treatment of amizyl intoxication. 3 references. (Journal abstract modified)

223064 Burov, Yu. V.; Salimov, R. M. Laboratoriya farmakoterapii ekstremal'nykh sostoyaniy, Otdela farmakologii, Instituta farmakologii, AMN SSSR, Moscow **/The effect of**

drugs on intraspecies aggression./ Vliyaniye farmakologicheskikh veshchestv na vnutrividovuyu agressiyu. Byulleten' eksperimental'noy biologii i meditsiny (Moskva). 79(5):64-67, 1975.

The effects of tranquilizers and sedatives on intraspecies aggression were investigated in rats. Aggression was elicited by forcing the rats to fight for territorial possession of a stool. Stelazine, haloperidol, amitriptyline, imipramine, chlordiazepoxide, diazepam and benactylzine were found to have tranquilizing effects on intraspecies aggression. Pentobarbitol and chlorpromazine had a sedative effect on aggression. 13 references. (Journal abstract modified)

223093 Jones, Byron C.; Consroe, Paul F.; Akins, Faren. Department of Pharmacology and Toxicology, University of Arizona, Tucson, AZ 85721 **Physostigmine-induced reversal of EEG and behavioral effects of delta9-tetrahydrocannabinol.** Bulletin of the Psychonomic Society. 6(2):204-206, 1975.

The effects of delta9-tetrahydrocannabinol (delta9-THC) in combination with physostigmine (PHYSO) on the electroencephalogram (EEG) and behavior were measured in adult unrestrained rabbits. The increase in mean cortical electrogenesis (voltage output) of the EEG induced by delta9-THC was clearly reversed by PHYSO. Hippocampal theta rhythm disrupted by delta9-THC was restored by PHYSO. Physostigmine also antagonized delta9-THC induced alteration of postural and activity behaviors. Except for very brief periods of retching, no behavioral indications of toxicity were observed. 12 references. (Author abstract)

223254 Domjan, Michael. Psychology Department, University of Texas, Austin, TX 78712 **Poison-induced neophobia in rats: role of stimulus generalization of conditioned taste aversions.** Animal Learning & Behavior. 3(3):205-211, 1975.

Rats repeatedly injected with lithium chloride were subsequently tested drinking novel and familiar solutions of both casein hydrolysate and vinegar. Injections in the absence of edibles result in only a small, and sometimes not reliable, increased avoidance of the novel casein and vinegar solutions. In contrast, if Ss acquired an aversion to saccharin as a result of the lithium injections, this learned aversion generalized to casein hydrolysate, with the generalization greatly enhanced by novelty of the casein flavor. However, the saccharin aversions did not generalize to the novel vinegar solution nearly as much as to the novel casein flavor. Results suggest that previous observations of poison induced neophobia were probably in part a result of the stimulus generalization of conditioned taste aversions, and that in addition to test stimulus novelty, some other factor, such as stimulus salience or similarity to the conditioned aversive flavor, is also involved in the generalization of learned tast aversions. 11 references. (Author abstract)

223563 Tessel, Richard Earl. University of Michigan **Relationships between the structure and the chronotropic, locomotor-stimulant and reinforcing actions of several fenfluramine analogs. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-10314 HC$13.50 MF$5.00 106 p.

Relationships between the structure and the chronotropic, locomotor stimulant and reinforcing actions of several fenfluramine analogs (n-ethyl amphetamine and its meta fluoro, chloro, bromo, iodo, methoxy, nitro, hydroxy, methyl and t-butyl derivatives) were examined, together with those of fenfluramine on locomotor activity in mice and on the rate of spontaneous beating of isolated guinea pig atria. Findings indicate that the maxima to which these compounds increased atrial rate and locomotor activity were inversely related to meta substituent steric effects. Neither hydrophobic nor electronic substituent effects contributed significantly to these relationships. Meta substituent variation also changed the maximal response rates that were maintained by response contingent injections of several of these derivatives, and the potencies with which these compounds maintained maximal rates, suppressed food reinforced responding and stimulated locomotor activity. Finally, the interactions of pargyline, reserpine and alpha-methyl-para-tyrosine methyl ester pretreatments with the effects of these amphetamine derivatives suggest that the latter drugs increase locomotor activity in mice and guinea pig atrial rate through the same mechanism. (Journal abstract modified)

223711 Wirth, Philip Wayde. University of Mississippi **The effect of stimulants and opioids on sensory reinforcement in rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-10689 HC$13.50 MF$5.00 91 p.

The effects of stimulants and opioids on sensory reinforcement in rats were studied to assess the role of light reinforcement noted in previous experiments. In part one, amphetamine, cocaine and morphine were given in three doses to Ss responding for light reinforcement. Parts two and three investigated the effect of drugs on possible reinforcing effects of auditory and cardiovascular stimulation to determine the role of other possible sensory reinforcers, but no significant effects occurred. The positive results of the light reinforcement tests involving amphetamine and cocaine suggest a possible confounding variable in studies of intravenous self-administration of these drugs. Part four studied the role of light reinforcement during drug self-administration of amphetamine, cocaine, morphine and heroin. Results indicate that when the factors of drug contingency and light contingency were manipulated in a free operant design, much of the initial responding in amphetamine and cocaine self-administration was the result of light reinforcement, but light had no effect on either morphine or heroin self-administration. Implications of this finding for stimulant self-administration research are discussed. (Journal abstract modified)

223737 Griek, Barbara Jeanne. University of Colorado **Cross tolerance between morphine and alcohol. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-3836 HC$13.50 MF$5.00 110 p.

Cross-tolerance between morphine and alcohol was examined in C57B1/6J and DBA/2J mice. All Ss of both strains receiving prolonged forced oral consumption of ethanol or morphine showed tolerance to the treatment drug. DBA/2J mice treated with ethanol showed a cross-tolerance to sodium amobarbital and to morphine sulfate in every test of drug effect. Mice of this same genotype treated with morphine sulfate showed a cross-tolerance to ethanol, but not to the barbiturate. Higher blood levels of ethanol were found at the time of loss of the righting reflex in Ss of both genotypes which had been treated with either ethanol or morphine, indicating that tolerance and cross-tolerance to ethanol are probably functional in nature. The C57B1/6J mice undergoing treatment with either drug regained the righting reflex at a higher blood concentration of ethanol than controls. DBA/2J mice, regardless of treatment, regained the righting reflex at the same blood level of ethanol, indicating that tolerance and cross-tolerance to ethanol in these Ss may be partly dispositional in nature. (Journal abstract modified)

223849 Stewart, Warren J. Department of Psychology, La Trobe University, Bundoora, Victoria, Australia **Size of the environment as a determiner of effects of scopolamine.** Psychological Reports. 37(1):175-178, 1975.

The effect of environment size was assessed on unconditioned responses in saline and scopolamine treated female albino rats. Ss were injected with either saline or 0.25 mg/kg scopolamine and tested in one of four different sized openfields. There was a positive correlation between increasing field size and increased ambulation in rats in the two smaller fields but not in the larger two fields; it did not attenuate the rate of habituation. Rearing and grooming were not affected so much by field size, but grooming was increased by scopolamine. The results are interpreted in terms of base rate/response competition hypotheses. 7 references. (Author abstract)

224466 Poletayeva, I. I.; Oleynik, V. M. Moskovskogo gosudarstvennogo universiteta im. M. V. Lomonosova, Moscow **/The influence of phenamine and caffeine on the capacity for extrapolation in rats.** Vliyaniye fenamina i kofeina na sposobnost' k ekstrapolyatsii u krys. Zhurnal vysshey nervnoy deyatel'nosti imeni I. P. Pavlova (Moskva). 25(3):529-534, 1975.

The effect of phenamine and caffeine on the ability to solve extrapolation problems was investigated in 28 albino and 68 hybrid rats. Success in searching for food after the disappearance of the alimentary stimulus from the rat's sight was measured both prior to and following drug administration. Neither caffeine nor phenamine administration was found to change the number of correct solutions, but they both diminished the number of refusals to solve the problem. A decrease in the number of refusals was achieved by increased motor activity and diminished rat emotionality during drug administration. Phenamine administration also facilitated the conditioning process, thus contributing to a greater number of positive solutions in a repeatedly presented task. 8 references. (Journal abstract modified)

224467 Arushanyan, E. B.; Baturin, V. A. Meditsinskogo instituta, Chita, U.S.S.R. **/The influence of phenamine on the avoidance reaction in intact and striatectomized rats./** Vliyaniye fenamina na reaktsiyu izbeganiya u intaktnykh i striatektomirovannykh krys. Zhurnal vysshey nervnoy deyatel'nosti imeni I. P. Pavlova (Moskva). 25(3):535-540, 1975.

The effect of phenamine on a conditioned avoidance reaction in a Y-maze was investigated in intact and striatectomized rats. Electric shocks were used to condition the rats to avoid one of the maze chambers. Phenamine administration in small doses of 0.5mg/kg facilitated the avoidance response, whereas large doses of 5 mg/kg dulled the response. Following ablation of the rostral parts of the striatum, small doses of the drug continued to facilitate the reaction, but the larger doses of the drug no longer dulled the responses. It is concluded that this behavior disturbance is related to the capacity of phenamine for activating nigrostriatal dopaminergic transmission. 18 references. (Journal abstract modified)

224504 Dyck, Dennis G.; Lussier, Don; Ossenkopp, Klaus-Peter. Dept. of Psychology, University of Manitoba, Winnipeg, Manitoba R3T 2N2 **The partial punishment effect following minimal acquisition training: sodium amobarbital and the stimulus properties of early punished trials.** Learning and Motivation. 6(3):412-420, 1975.

In a runway investigation, six groups of rats received limited runway training such that partial punishment, partial reinforcement, or continuous reinforcement was accompanied by sodium amobarbital or saline. Following an interpolated phase of continuous reinforcement without injections, all groups were given punished extinction. It was found that partial punishment increased resistance to punished extinction relative to partially and continuously reinforced controls when acquisition was given under saline. When partial punishment training was accompanied by amobarbital this effect was eliminated. The drug was observed to have no effect on the punished extinction performance of the partial reinforcement and continuous groups, respectively. Moreover, the partial reinforcement effect did not generalize to punished extinction. These data provide information concerning the difference between the stimuli associated with the early trials of punishment and nonreward and indicate that the former but not the latter contain emotional elements. 11 references. (Author abstract modified)

224776 Noble, Adele B.; McKinney, William T., Jr.; Mohr, Carol. Department of Psychiatry, University of Wisconsin Medical School, Madison, WI, 53706 **Diazepam treatment of socially isolated monkeys.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, DC, American Psychiatric Assn., 1975. 354 p. (p. 102-103).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, May 1975, a paper was presented which reported on the effects of diazepam treatment of socially isolated monkeys. A pilot study first used diazepam to treat Ss 1 and 1.5years postisolation who were exhibiting typical isolate behaviors. Five of the six Ss showed a decrease in one or more of their predominant self-disturbance behaviors. Based on these data, three more rhesus monkeys were placed in total isolation for the first 7 months of their lives, and diazepam treatment was started during the last 4 weeks they were in the chambers. Treatment continued after removal and during 16 weeks of social testing. A dramatic decrease in the self-disturbance behaviors occurred in two of the Ss and, in addition, an increase in environmental and social behaviors was observed. The third S was a nonresponder at the doses used. Findings indicate that a socially induced syndrome could be reversed by social and pharmacologic methods, and that social isolation failed to produce psychosis models but did produce a less specific fear anxiety syndrome which when lowered in a nonspecific manner produced behavioral improvement. (Journal abstract modified)

224906 Janowsky, David S.; Meacham, Martin; Blaine, Jack; Schorr, Michael; Bozzetti, Louis. Department of Psychiatry, University of California, San Diego, CA **Effects of marijuana on flying ability.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatry Assn., 1975. 354 p. (p. 251-252).

At the 128th Annual Meeting of the American Psychiatric Association, Anaheim, California, May 1975, a paper was presented reporting the results of studying the effects of marihuana intoxication on the ability of certificated pilots to operate a general aviation model ATC-510 instrument flight simulator. Three professional and three private pilots were included who had been smoking marihuana for several years and could be described as infrequent users. Results indciate that smoking marihuana in socially used doses causes dramatic detrioration of simulated instrument flying ability. Intoxication is therefore incompatible with safe aircraft operation. More generally, it causes a signfiicant and profound deterioration in psychomotor ability when a person is required to perform

simultaneously a series of tasks requiring memory and attention to multiple tasks performed over time in three dimensions. (Journal abstract modified)

224907 Miller, Robert E.; Deets, Allyn C. Department of Psychiatry, Western Psychiatric Institute and Clinic, Pittsburgh, PA **Delta-nine-THC and non-verbal communication in monkeys.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 253-254).

At the 128th Annual Meeting of the American Psychiatric Association, Anaheim, California, May 1975, a paper was presented reporting the results of testing the influence of delta9-tetrahydrocannabinol (THC) on nonverbal communication of affect and free social behavior in a group of six young, male rhesus monkeys. Results indicate that delta9-THC affects social communication in a complex fashion. Administration of the drug to the stimulus animal disrupted nonverbal communication when the responder was undrugged, but not when he had also received delta9-THC. THC enhanced the nonverbal sensitivity of drugged responders irrespective of the drug state of the stimulus monkey. While it had no effect on either basal or conditioned cardiac responses of stimulus monkeys, it significantly reduced basal levels of heartrate in responders and enhanced conditioned cardiac response to a trial presentation. It is concluded that pharmacological agents which alter expressiveness or sensitivity of affective cues from others also elicit changes in the social interactions and role relationships within the social group. Stimulants, tranquilizers, and hallucinogens have discriminably different effects on nonverbal communication and group social behavior. (Journal abstract modified)

225077 Sobrian, Sonya K.; Weltman, Mardi; Pappas, Bruce A. Dept. of Psychology, Carleton University, Ottawa, Ontario, K1S 5B6, Canada **Neonatal locomotor and long-term behavioral effects of d-amphetamine in the rat.** Developmental Psychobiology. 8(3):241-250, 1975.

The effects of d-amphetamine on locomotor activity in the neonatal rat and on the behavior of rats given adult amphetamine during the infancy period were examined. Locomotor activity in the neonate was found to increase from birth until the beginning of the third week of life, at which time it peaked and then subsequently declined. Subcutaneous injections of both 0.25 and 2.0mg/kg of amphetamine increased activity in rats 1-21 days of age with the maximum effect observed at 4 days of age. No tolerance to amphetamine was observed after six daily injections beginning at 1, 7, or 14 days of age. The decline in the excitatory effects of the drug thus reflected maturational changes in response to it. No persisting effects of the neonatal drug treatment were observed on adult two-way avoidance learning. 15 references. (Author abstract modified)

225079 Seliger, Deborah Levy. Dept. of Psychology, Rutgers University, Camden, NJ 08102 **Prenatal maternal d-amphetamine effects on emotionality and audiogenic seizure susceptibility of rat offspring.** Developmental Psychobiology. 8(3):261-268, 1975.

In a study of the effects of prenatal maternal d-amphetamine on emotionality and susceptibility to audiogenic seizures (SA) in the offspring, dosages of 0, 5 and 10mg/kg of amphetamine were injected s.cto gravid rats during days 5-9 or 12-16 of gestation. Offspring were assessed for water wading emotionality and AS behaviors. No significant differences among groups were found in defecation scores (a measure of emotionality) from either test. The only animals to exhibit a considerable incidence of wild running attacks or seizures were those whose mothers had received the placebo early in pregnancy. The differences are judged to be consistent with most findings that indicate an enhancement of immunity to AS susceptibility as a function of prior stress. 13 references. (Author abstract modified)

225081 Randt, Clark T.; Blizard, David A.; Friedman, Eitan. Dept. of Neurology, School of Medicine, New York University, 550 First Ave., New York, NY 10016 **Early life undernutrition and aggression in two mouse strains.** Developmental Psychobiology. 8(3):275-279, 1975.

The effect of early undernutrition on aggressive behavior was examined in two strains of mice, C57BL/6J and DBA/2J. Because serotonin (5-hydroxytryptamine, 5-HT) was previously implicated in the manifestation of aggressive behavior, the effects of early undernutrition on 5-HT and its metabolite, 5-hydroxyindoleacetic acid (5-HIAA), were also studied. Early undernutrition was shown to be correlated with increased aggression in adult mice after isolation. This was significant in numbers of fights and shorter latency to fight in the DBA/2J strain. Lower brain levels of 5-HIAA after pretreatment with a monoamine oxidase inhibitor were found in the undernourished group. 13 references. (Author abstract modified)

225149 Sanger, D. J.; Blackman, D. E. Dept. of Psychology, University of Birmingham, P.O. Box 363, Birmingham B15 2TT, England **The effects of chlordiazepoxide on the development of adjunctive drinking in rats.** Quarterly Journal of Experimental Psychology (Cambridge). 27(3):499-505, 1975.

The effects of chronic administration of chlordiazepoxide (CDZ) on the the development of adjunctive drinking in rats, a pattern of behavior thought to be due to emotional arousal, were studied. Intermittent delivery of food pellets induces high levels of adjunctive drinking in rats. The chronic administration of CDZ did not prevent the development of adjunctive drinking after food pellets delivered at 1 min intervals. The drug was found to slightly enhance the development of drinking, an effect ascribed to the drug's ability to facilitate the performance of several patterns of responding. When CDZ was withdrawn, a disruption in the pattern of adjunctive drinking was observed. 25 references. (Author abstract modified)

225155 Weeks, James R. Experimental Biology Division, Upjohn Company, Kalamazoo, MI 49002 **Environmental influences affecting the voluntary intake of drugs: an overview.** Federation Proceedings. 34(9):1755-1758, 1975.

An overview of environmental influences affecting the voluntary intake of stimulant and depressant drugs in animals is presented. These factors include the dose, its schedule of administration and conditioning of drug administration to secondary cues. There are differences in drug administration of stimulants and depressants. There is an inverse relationship between the size of the dose and the number of injections taken, but for stimulants daily intake will remain constant whereas for depressants smaller doses are only partially compensated for by increased numbers of injections. Drug intake of stimulants is better maintained on ratio schedules. Neutral stimuli, such as lights or buzzers paired with drug injections, can be used to elicit conditioned responses. Such responses have been used to evaluate the reinforcing properties of drugs. 52 references. (Author abstract modified)

225156 Thompson, Travis; Pickens, Roy. University of Minnesota, Minneapolis, MN 55455 **An experimental analysis of behavioral factors in drug dependence.** Federation Proceedings. 34(9):1759-1770, 1975.

Behavioral consequences in drug self-administration in experimental situations are discussed, and procedures for studying responses due to self-administered drugs in animals are examined. Consideration is given to the nature of drug reinforcers, and inducing and noninducing procedures for acquisition of drug reinforced responding. Studies on maintenance of drug self-administration are examined, with emphasis on injection dose and schedule of drug presentation. Procedures for reducing or eliminating the control a reinforcing drug may have over behavior include: 1) weakening the reinforcing properties of the drug; 2) changing stimulus control of drug self-administration; and 3) increasing the probability of punishment associated with drug taking. Studies bearing on elimination are surveyed, and implications for humans are examined. 84 references.

225157 Goldberg, S. R.; Kelleher, R. T.; Morse, W. H. Laboratory of Psychobiology, Dept. of Psychiatry, Harvard Medical School, Boston, MA 02115 **Second-order schedules of drug injection.** Federation Proceedings. 34(9):1771-1776, 1975.

Operant techniques were used to study behavior maintained by drug injection in monkeys. Key press responding of squirrel monkeys produced intravenous injections of cocaine under fixed-ratio (FR) and fixed-interval (FI) schedules. Under an FI schedule, every 30th response produced an injection; steady responding at high rates of over one per second were maintained during each FR component. Under an FI schedule, the first response occurring after a fixed time of 5 minutes produced an injection; there was a pause at the start of each interval and then progressively increasing responding until cocaine was injected at the end of the interval. Under one type of second order schedule, completion of each FI component produced only a 2 sec light; completion of the tenth FI component produced the light and an intravenous injection of cocaine. Under a second type of second order schedule, each FR component completed during a fixed time interval produced only a brief light; the first FR component completed after the interval of time elapsed produced the light and intravenous or intramuscular injection of cocaine. 16 references. (Author abstract modified)

225159 Harvey, John A.; Schlosberg, Arthur J.; Yunger, Libby M. Dept. of Psychology, University of Iowa, Iowa City, IA 52242 **Behavioral correlates of serotonin depletion.** Federation Proceedings. 34(9):1796-1801, 1975.

Behavioral correlates of serotonin (5-hydroxytryptamine, 5-HT) depletion were examined in the rat after depletion of telencephalic 5-HT content by medial forebrain bundle lesions. Results indicate an increased sensitivity to pain as measured by the flinch jump, stabilimetric or hot plate methods. Examination of a number of other lesions and drugs indicated that dopamine, norepinephrine and acetylcholine are not involved in pain sensitivity. Taken together, data suggest that the serotonergic system normally acts to inhibit the effects of painful stimuli. A review of a variety of behavioral effects of 5-HT depletion including an enhanced response to lysergic acid diethylamide and amphetamine suggests that the ascending serotonergic system may have a general role in the inhibition of arousal, rather than a specific role with respect to various categories of behavior. 51 references. (Author abstract modified)

225160 Sparber, Sheldon B. Dept. of Pharmacology, University of Minnesota, Minneapolis, MN 55455 **Neurochemical changes associated with schedule-controlled behavior.** Federation Proceedings. 34(9):1802-1812, 1975.

By combining the technologies of radioisotope chemistry, operant behavior control and modification, and brain perfusion with push pull cannulas, minute to minute changes in the disposition of radiolabeled monoamine transmitter candidates and their metabolites were studied. These substances appear to covary with changes in complex behavior maintained by operant schedules of reinforcement and affected by changes in schedules or administration of psychotropic drugs. Changes in fractional distribution of radiolabeled urea were observed along with shifts in monoamines; but the former appear more transient. Findings support the concept of dynamic changes within the extracellular environment of the central nervous system that may be part of a hormone like communicating system with functional significance. The presence of peaks and/or troughs in perfusates of labeled urea or similar substances should not be taken as a priori evidence for nonspecificity of the technique since selective release or inhibition of release of monoamines can be shown with appropriate drugs that are thought to act through these aminergic systems. Destruction of catecholamine nerve terminals with 6-hydroxydopamine likewise attenuates the signal locked release of radiolabeled norepinephrine by a conditioned stimulus after conditioning occurs. 61 references. (Author abstract modified)

225161 Aprison, M. H.; Hingtgen, J. N.; McBride, W. J. Neurobiology Section, Institute of Psychiatric Research, Indiana University Medical Center, Indianapolis, IN 46202 **Serotonergic and cholinergic mechanisms during disruption of approach and avoidance behavior.** Federation Proceedings. 34(9):1813-1822, 1975.

Relationships between central nervous system transmitters and behavior were studied in rats and pigeons. Injections of D,L-5-hydroxytryptophan (D,L-5-HTP) on animals working on approach schedules produce a period of behavioral depression that is temporally correlated to increased levels of total serotonin (5-HT) in the telencephalon and diencephalon. Administration of alpha-methyl-meta-tyrosine (a-MMT) also resulted in depressed responding; however, the temporal correlation is with decreased levels of total 5-HT in brain. Similar behavioral disruptions resulting from these two apparently opposite biochemical states suggest that in both cases more 5-HT is released within certain key serotonergic synapses mediating this behavior. Evidence from subcellular studies supports this concept. Whereas serotonin appears to be involved in the disruption of approach behavior, studies indicate that acetylcholine may play a role in excitation during avoidance behavior. 32 references. (Author abstract modified)

225162 Seiden, L. S.; MacPhail, R. C.; Oglesby, M. W. University of Chicago, Chicago, IL 60637 **Catecholamines and drug-behavior interactions.** Federation Proceedings. 34(9):1823-1831, 1975.

Studies are reviewed which show that catecholamines are of functional importance in the maintenance of operant behavior and that operant responding, or some aspect of the operant situation affects catecholamine metabolism in the central nervous system (CNS). The fact that many drugs which exhibit drug - behavior interactions also produce characteristic effects on the metabolism of CNS catecholamines suggests that the performance of operant behavior per se modifies brain catecholamines metabolism and thereby the subsequent drug effect. Experiments measuring the depletion of catecholamines following synthesis inhibition with alpha-methyl-para-tyrosine (aMT), or changes in the specific activity of norepinephrine after tritium labeling, have shown that operant behavior alters the metabolism of catecholamines. Preliminary evidence is also

presented from experiments designed to determine variables associated with the performance induced changes in catecholamine metabolism. Results suggest a neurochemical mechanism for the rate dependent effects of amphetamine and aMT. 88 references. (Author abstract modified)

225169 McMillan, D. E. Department of Pharmacology, School of Medicine, University of North Carolina, Chapel Hill, NC 27514 **Determinants of drug effects on punished responding.** Federation Proceedings. 34(9):1870-1879, 1975.

The experimental variables which determine the effects of drugs on punished responding in animals are reviewed. Among these variables are the drug history of the animal, the dose of the drug administered, the type of stimulus used to punish responding, the intensity and duration of the punishing stimulus, the schedule of presentation of the punishing stimulus, the control rate and pattern of punished responding, the species of animal, the behavioral history of the animal and the nature of the required response. Although it is not known how all of these variables interact to determine the effect of drugs on punished responding, there is evidence that many of these variables are important determinants of drug effects. The task facing behavioral pharmacologists studying drug effects on punished responding is to determine under what conditions drugs produce their characteristic effects on these responses. 43 references. (Author abstract modified)

225170 Laties, Victor G. Department of Radiation Biology and Biophysics, University of Rochester, Rochester, NY 14642 **The role of discriminative stimuli in modulating drug action.** Federation Proceedings. 34(9):1880-1888, 1975.

Pecking studies in piegeons trained on fixed interval schedules which have shown that the nature of the controlling (discriminative) stimulus can govern the degree to which drugs change performance are reviewed. Scopolamine and amphetamine show the most pronounced interaction with level of stimulus control; when stimulus control is strong, the drug effects are minimal and when control is weak, the drug effects are greater. Chlorpromazine and promazine are relatively insensitive to changes along this dimension. In general, findings of studies using other schedules of reinforcement support the conclusion that behavior under strong external stimulus control is less apt to be readily affected by many drugs. Addition of the discriminative stimulus can also "improve" the behavior of pigeons that have been given enough methylmercury to increase greatly the variabilithy of their performance. 40 references. (Author abstract modified)

225171 Cook, Leonard; Sepinwall, Jerry. Dept. of Pharmacology, Research Division, Hoffmann-LaRoche Inc., Nutley, NJ 07110 **Reinforcement schedules and extrapolations to humans from animals in behavioral pharmacology.** Federation Proceedings. 34(9):1889-1897, 1975.

Psychotherapeutically important drugs are discussed in terms of the schedules of reinforcement that best measure their behavioral effects. Conditioned avoidance techniques have been useful for studying neuroleptics and for predicting their clinical antipsychotic activity; the possible involvement of dopaminergic mechanisms in the effects of neuroleptics on avoidance behavior is discussed. Tricyclic antidepressant agents have been studied in assays involving interactions with other agents. Sidman avoidance has been a sensitive assay for such drug interactions. A schedule in which observing responses in pigeons are measured seems to provide a method for studying antidepressants without involving drug interaction phenomena. For tricyclic compounds, facilitation of observing responses and weak potency of conditioned avoidance inhibition constitute a pharmacological profile that seems to have some predictive value for clinical imipramine like antidepressant activity. Conflict schedules have been useful for predicing antianxiety activity in man. 54 references. (Author abstract modified)

225172 Heise, George A. Department of Psychology, Indiana University, Bloomington, IN 47405 **Discrete trial analysis of drug action.** Federation Proceedings. 34(9):1898-1903, 1975.

The use of discrete trial procedures is illustrated in an examination of the effects of scopolamine on several aspects of behavior: memory, inhibition and discrimination. Response alternation experiments show that, whereas accuracy of responding is consistently poorer under drug, the decline of accuracy with time since the last trial is similar for drugged and nondrugged animals. Experiments in which discrete trials are presented in pairs, such that the correct response on trial two of the pair is contingent upon trial one events, show how the disinhibiting effect of scopolamine is augmented by increasing the time gap between trials. A variety of experiments suggest that scopolamine decreases the detectability of stimuli. Detectability effects, along with disinhibition observed under specific conditions, constitute the principal behavioral actions of the drug observed with discrete trial procedures. 15 references. (Author abstract modified)

225287 Green, R. A.; Gillin, J. C.; Wyatt, R. J. Lab. of Clinical Psychopharm. Div. of Special Mental Health Res., NIMH, St. Elizabeths Hospital, DC 20032 **The effect of intraventricular administration of serotonin on spontaneous motor activity of rats. (Unpublished paper).** Washington, DC, NIMH, 1975. 9 p.

Spontaneous motor activity was studied following intracerebral injections of 1, 10 and 50 micrograms of serotonin (5-HT) into the lateral ventricle of surgically cannulated rats. These data were compared to data from rats given saline with and without pargyline pretreatment. During the first 15 minutes, the rats receiving the higher doses of 5-HT showed significant decrements in motor activity compared to saline controls. Pargyline pretreated rats showed similar decrements in motor activity. No activation was observed in either group. After 20 minutes, no significant differences for any treatment condition compared to saline controls were observed. It is concluded that a principal effect of directly increasing brain 5-HT concentration is to decrease activity. Possible mechanisms for this effect are discussed. 22 references. (Author abstract)

225557 Castellano, Claudio; Oliverio, Alberto. Laboratorio di Psicobiologia e Psicofarmacologia, Via Reno 1, I-00198 Rome **A genetic analysis of morphine-induced running and analgesia in the mouse.** Psychopharmacologia (Berlin). 41(3):197-200, 1975.

A genetic analysis of morphine induced analgesia and activity was conducted in mice of the BALB/cJ, C57BL/6J, DBA/2J strains, and to their F1 and backcross progenies. The results support previous findings showing that a negative correlation is evident between these two behavioral measures and that their mode of inheritance is characterized by dominance or partial dominance. The biometric analysis conducted on the parental F1 hybrid and backcross populations indicates that the effects of morphine are genetically determined. 10 references. (Author abstract modified)

225559 Munster, G.; Battig, K. Swiss Federal Institute of Technology, CH-8006 Zurich, Switzerland **Nicotine-induced hypophagia and hypodipsia in deprived and in hypothalamically stimulated rats.** Psychopharmacologia (Berlin). 41(3):211-217, 1975.

Results indicate that tests on nicotine, in doses of 0.15 and of 0.45 mg/kg, induced hypophagia and hypodipsia in 20 hours deprived rats and elevated the threshold currents for hypothalamically induced feeding and drinking in satiated rats. These effects were blocked by pretreatment with .05 mg/kg mecamylamine, but not by pretreatment with 3.0or 9.0mg/kg hexamethonium. These results indicate a centrally located mechanism for the hypophagic and hypodipsic effect of single injections of nicotine. 34 references. (Journal abstract modified)

225560 Glick, S. D.; Cox, R. S.; Crane, A. M. Mount Sinai School of Medicine, City University of New York, New York, NY 10029 **Changes in morphine self-administration and morphine dependence after lesions of the caudate nucleus in rats.** Psychopharmacologia (Berlin). 41(3):219-224, 1975.

Changes in morphine self-administration and morphine dependence after lesions of the caudate nucleus in rats were experimentally produced. Rats were trained to bar-press for intravenous infusions of morphine sulfate during 1 hour daily test sessions. Small, centrally located bilateral lesions of the caudate nucleus reduced rates of morphine self-administration to approximately 1/7 of preoperative levels. Caudate lesions also lowered the threshold dose at which morphine's rewarding property could be detected. Physical dependence was studied in other rats receiving a 3 day continuous infusion of morphine sulfate via implanted subcutaneous silicone reservoirs. Caudate lesions ameliorated withdrawal induced weight loss and naloxone induced shakes. Results of the morphine self-administration and dependence data support the hypothesis that morphine blocks dopaminergic transmission in the striatum. 12 references. (Journal abstract modified)

225561 Johansson, Jan O.; Jarbe, Torbjorn U. C. Dept. of Psychology, University of Uppsala, Slottsgrand 3, S-75220 Uppsala, Sweden **Antagonism of pentobarbital induced discrimination in the gerbil.** Psychopharmacologia (Berlin). 41(3):225-228, 1975.

An experimental study examined whether differential responding in a T-maze would appear when gerbils were required to differentiate apentobarbital and bemegride mixture from a saline condition (group 2) from the start of the discriminative training. The acquisition rate for this group was compared with that of another group which was required to discriminate the barbiturate alone from the no drug condition (group 1). Bemegride, and metrazol, but not cocaine, antagonized the pentobarbital produced discimination. It was concluded that a bemigrade/phenobarbital mixture produces a state similar to that created by the nondrug state and therefore could not be discriminated by the gerbils. 15 references. (Author abstract modified)

225563 Coyle, I. R.; Singer, G. Dept. of Psychology, La Trobe University, Bundoora, Victoria, Australia 3083 **The interaction of post-weaning housing conditions and prenatal drug effects on behaviour.** Psychopharmacologia (Berlin). 41(3):237-244, 1975.

The interaction of postweaning housing conditions and prenatal drug effects on behavior was experimentally tested. Offspring of rats given oral doses of imipramine from 14 to 21 days prior to mating until parturition or vitamin A between days 8 and 10 of gestation were reared after weaning in deprived or enriched environments. When tested in both a Henderson type maze and a swimming maze, no behavioral effects due to prenatal drug exposure were observed in the subjects reared in a deprived environment. When the subjects were reared in an enriched environment, the maze performance of animals that had been exposed to imipramine or vitamin A was significantly inferior to that of the controls. The implications of results are discussed with respect to environmental interaction with prenatal drug effects on behavior. 27 references. (Author abstract modified)

225564 Torre, Michele; Torre, Eugenio; Bogetto, Filippo. University of Turin, Via Cherasco 15, I-10126 Torino, Italy **The relation between cerebral serotonin levels and conditioned behaviour in the rat following the administration of LSD-25 and UML.** Psychopharmacologia (Berlin). 41(3):245-247, 1975.

The relation between cerebral serotonin levels and conditioned behavior in the rat following administration of lysergic acid diethylamide (LSD-25) and 1-Methyl-d-lysergic acid butanolamide (UML) was experimentally studied. Successive daily injections of LSD-25 and UML caused progressive depression of brain 5HT levels in the rat. The decrease was significant on the 4th day with respect to the highly significant fall observed after a single administration, whereas it was shown previously that conditioned behavior is no longer affected by LSD-25 after three days and that simultaneous administration of single doses of LSD-25 and UML is equally ineffective in this respect. Its depression of 5HT levels by LSD-25 and UML was shown to be equal to that of LSD-25 alone at doses that influence conditioned behavior. It was concluded that changes in such behavior are not dependent on brain 5HT levels and that no link exists between such levels and the psychotomimetic effect of LSD-25 in man. 8 references. (Journal abstract modified)

225566 Houser, Vincent P.; Cash, Randall J. Veterans Administration Hospital, Perry Point, MD 21902 **The effects of chronic morphine administration upon a modified Sidman avoidance schedule that utilizes response-independent shock.** Psychopharmacologia (Berlin). 41(3):255-262, 1975.

The effects of chronic morphine administration on a modified Sidman avoidance schedule utilizing response independent shock were studied experimentally in six male squirrel monkeys. Both facilitated and suppressed avoidance response rates observed during superimposed 3 minute conditioned stimuli (CS) unavoidable shock pairings were altered by administration of morphine sulphate. Morphine also led to a reliable reduction in overall response rate and an increase in shocks received. It was concluded that a potent analgesic agent such as morphine may be able to reduce the level of fear motivation normally generated by aversive CS. 25 references. (Author abstract modified)

225568 Gianutsos, Gerald; Lal, Harbans. University of Rhode Island, Kingston, RI 02881 **Effect of loperamide, haloperidol and methadone in rats trained to discriminate morphine from saline.** Psychopharmacologia (Berlin). 41(3):267-270, 1975.

The effect of loperamide, haloperiodol, and methadone was tested in rats trained to respond differentially in an operant procedure of lever pressing at FR10 schedule of food reinforcement in order to discriminate the effects of morphine injection from those of saline injection. Rats reliably emitted responses cuing morphine except in small oral doses. After either loperamide or haloperidol doses the rats responded as though saline had been given. It is suggested that specific central effects produced only by narcotic analgesics are the basis for these morphine cues. 15 references. (Author abstract modified)

05 TOXICOLOGY AND SIDE EFFECTS

215160 Nieminen, L.; Mottonen, M.; Arvela, P. Research Center Laake-Medipolar, Box 425, SF-20101 Turku 10, Finland **The effect of cold and diazepam on the toxicity of fenfluramine in mice.** Experientia (Basel). 31(3):338-339, 1975.

The effectiveness of cold treatment, diazepam, and practolol in the treatment of fenfluramine intoxication was studied in mice. It was found that cold treatment decreased or abolished the hyperactivity and convulsions caused by fenfluramine. A diazepam dose of only 0.2mg/kg decreased the toxicity of fenfluramine significantly, while a dose of 2.0mg/kg abolished convulsions and hyperactivity. Only a very high dose (5mg/kg) of practolol could decrease toxic effects. These results suggest that diazepam and cold treatment given as early as possible decrease the toxicity of fenfluramine also in humans and especially in children, while practolol may have no clinical application. 7 references.

215695 Bellwinkel, S.; Schafer, A.; Minne, H.; Ziegler, R. Department of Endocrinology and Metabolism, Center of Internal Medicine and Pediatrics, University of Ulm, Ulm, Germany **The effect of chronic lithium application on the mineral content of rat bone and soft tissues.** International Pharmacopsychiatry (Basel). 10(1):9-16, 1975.

The effects of chronic lithium treatment were studied in rats treated with lithium chloride over 6 weeks. During the experiment, determinations of serum calcium, magnesium and phosphorus revealed no changes due to the therapy. Postmortem examinations of liver, skeletal muscle, and femur minerals as well as bone histology showed these organs to be unaffected by lithium application. Only body weight gain was in part increased by lithium. 28 references. (Author abstract)

217518 Rosenkrantz, Harris; Sprague, Rosa A.; Fleischman, Robert W.; Braude, Monique C. Mason Research Institute, Worcester, MA 01608 **Oral delta9-tetrahydrocannabinol toxicity in rats treated up to six months.** Toxicology and Applied Pharmacology. 32(2):399-417, 1975.

Chronic toxicity of delta9-tetrahydrocannabinol (THC) given orally 28, 90, and 180 days to Fischer rats at doses of 2, 10, and 50 mg/kg was investigated. In the first 10 days central nervous system (CNS) depression, incoordination, ataxia and passivity, poikilothermia, and hypopnea occurred to which tolerance developed. During days 10-20, irritability, hypersensitivity, hyperactivity, and aggression predominated. Fighting occurred between days 20-100. Tremors and clonic convulsions appeared after day 70 in 50% of the animals at 50mg/kg and 12% at 10mg/kg. Tolerance developed to CNS stimulation, fighting and neurotoxicity and lethal cumulative toxicity was seen although the cause of death was not established. Growth rate of both sexes was inhibited despite an elevation in food consumption after a transient anorexia. 29 references. (Author abstract modified)

217578 Nichols, D. E.; Ilhan, M.; Long, J. P. Department of Medicinal Chemistry, School of Pharmacy and Pharmaceutical Sciences, Purdue University, West Lafayette, IN 47907 **Comparison of cardiovascular, hyperthermic, and toxic effects of para-methoxyamphetamine (PMA) and 3,4-methylenedioxyamphetamine (MDA).** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 214(1):133-140, 1975.

The cardiovascular, hyperthermic and toxic effects of paramethoxyamphetamine (PMA) and 3,4-methylenedioxyamphetamine (MDA) were examined. Both PMA and MDA had potent stimulatory effects on mean arterial blood pressure and heartrate in the cat. These effects were antagonized by bretylium, a compound which blocks release of norepinephrine. The increases in heartrate were also antagnozized by propranolol and the blood pressure increases by phenoxybenzamine. PMA and MDA were nearly equipotent. In male albino mice, determination of 6 hr LD50's indicated PMA to be most toxic although 24 hr LD50's showed nearly equal toxicity. MDA had a potent hyperthermic effect in mice which was partially antagonized by bretylium and was blocked by haloperidol. The hyperthermic effect of PMA was not as pronounced and was followed by hypothermia. 16 references. (Author abstract)

217694 Miller, Richard P.; Becker, Bernard A. Department of Pharmacology, College of Medicine, University of Iowa, Iowa City, IA 52242 **Teratogenicity of oral diazepam and diphenylhydantoin in mice.** Toxicology and Applied Pharmacology. 32(1):53-61, 1975.

The effects upon the offspring of mice treated orally with diazepam (DAP) or diphenylhydantoin (DPH) during pregnancy were studied. Significant increases of cleft palates over controls were found in offspring following 3 day maternal administration of DAP, 140 mg/kg and DPH, 87.5or 125 mg/kg on days 11 to 13; and single day administration of DAP 400mg/kg on days 11 to 14; and of DAP, 500mg/kg and DPG, 125mg/kg on days 11 to 15. There was a greater incidence of significant increases of resorptions and significantly depressed fetal bodyweights following single day administration of DAP, 500mg/kg than after all other treatments. In conclusion, oral DPH and oral DAP, at a higher dosage level, produce a similar teratogenic effect, cleft palate, in the mouse. 18 references. (Author abstract modified)

217697 Thomas, Robert J. Department of Anatomy, School of Medicine, Creighton University, Omaha, NB 68178 **The toxicologic and teratologic effects of delta9-tetrahydrocannabinol in the Zebrafish embryo.** Toxicology and Applied Pharmacology. 32(1):184-190, 1975.

The toxicologic and teratologic effects of delta9-tetrahydrocannabinol (THC) in the Zebrafish (Brachydanio rerio) embryos were examined. Embryos at late high blastula were exposed to tetrahydrocannabinol at 1.0to 10.0ppm of aquarial media. There was no cytotoxicity or significant embryo loss after exposure for 24 hr at any tested concentration of THC. After 24 hr, there was a statistically significant reduction of spontaneous tail muscle twitch (at the normal time of its development) and subsequent embryo death above 2.0ppm THC. No effect on spontaneous muscle twitch or any subsequent death of embryos at 2.0ppm THC, but 37% distal trunk anomalies and no identifiable effect or death below 2.0ppm THC were observed. 18 references. (Author abstract)

217880 Basu, P.; Kramer, P. F.; Feller, D. R. College of Pharmacy, Division of Pharmacology, Ohio State University, Columbus, OH 43210 **Correlation of (+)-amphetamine lethality and hepatic metabolism.** Journal of Pharmacy and Pharmacology (London). 26(11):910-911, 1974.

A correlation of (+)-amphetamine lethality and hepatic metabolism is presented. Pretreatment with spironolactone did not alter the rate of (+)-amphetamine disappearance at 0.33 mM, but completely abolished the reduction in microsomal metabolism at 0.67 mM in the control preparation. In contrast, the prior administration of phenobarbitone did not modify the rates of amphetamine disappearance at either dose level when compared with the rates obtained in control microsomes. The

data show that qualitatively similar dose dependent patterns are observed with hepatic biotransformation and lethality of (+)-amphetamine in CF-1 mice. While (-)-amphetamine exhibited a triphasic response in hepatic microsomal metabolism, this isomer gave only a single LD50 value. These findings suggest the need for additional in vivo and in vitro experiments to clarify the relation between amphetamine biotransformation and lethality. 11 references.

220950 Iverson, F.; Coldwell, B. B.; Downie, R. H.; Whitehouse, L. W. Drug Research Laboratories, Health Protection Branch, Health and Welfare Canada, Tunney's Pasture, Ottawa K1A 0L2, Canada **Effect of ethanol on toxicity and metabolism of amphetamine in the mouse.** Experientia (Basel). 31(6):679-680, 1975.

The effect of ethanol on the toxicity and urinary metabolite profile on amphetamine was examined in the mouse. Ethanol at 3gm/kg i.p. did not significantly alter the acute toxicity of amphetamine in the mouse. However, the urinary metabolite pattern was changed, suggesting that ethanol suppressed metabolism of amphetamine during the initial 6 hr period. After 24 hr, the mouse metabolized the same fraction of a given dose of amphetamine, whether it was given alone or in combination with 2, 3, or 4 gm/kg ethanol. 13 references. (Author abstract modified)

223015 Lavretskaya, E. F.; Moshkovskiy, Yu. Sh.; Raykhman, L. M. Nauchno-issledovatel'skiy institut po biologicheskim ispytaniyam khimicheskikh soedineniy, Kupavna Moskovskoy oblasti, Moscow **/The effect of psychotropic and anticonvulsive drugs on the transport of ATP-ase in the renal tubes of a guinea-pig./** Vliyaniye psikhotropnykh i protivosudorozhnykh preparatov na transportnuyu ATF-azu pochechnykh kanal'tsev morskoy svinski. Farmakologiya i Toksikologiya (Moskva). 38(3):272-275, 1975.

The effect of neuroleptics, tricyclic antidepressants, somnifacients and antiepileptics on the transport of adenosine triphosphatase (ATPase) and p-nitrophenylphosphatase from the renal tubules was investigated in guinea-pigs. Neuroleptics in high concentrations were found to almost completely suppress the activity of the ATPase, but had little effect on p-nitrophenlyphosphatase activity. The butyrophenone derivatives had a mild suppression effect on p-nitrophenylphosphatase activity when used in large doses, and a stimulating effect when used in low concentrations. The effect of the tricyclic antidepressants was similar to that of the phenothiazine neuroleptics. Lithium carbonate had no effect on enzyme activity. Barbiturates and antiepileptic agents mildly inhibited both enzymes. 20 references. (Journal abstract modified)

223019 Vorontsov, V. V. Altayskogo meditsinskogo instituta Barnaul, Khazakhstan, U.S.S.R. **/The influence of some phenothiazine derivatives on renal function./** Vliyaniye nekotorykh proizvodnykh fenotiazina na funktsiyu pochek. Farmakologiya i Toksikologiya (Moskva). 38(3):313-316, 1975.

The effect of phenothiazine derivatives on renal function was investigated in rats and dogs. Prolonged exposure to chlorathizin and chlormorphathizin were found to elicit substantial diuretic and saluretic action in both rats and dogs. Fluorathizin and imizine were found to inhibit urinary flow. Diprazine augmented urinary output in dogs, but depressed output in rats. The new antidepressive drug, azaphen, did not have any marked effect on urinary flow. 11 references. (Journal abstract modified)

225165 Schuster, Charles R.; Fischman, Marian W. Dept. of Psychiatry, University of Chicago Pritzker School of Medicine, Chicago, IL 60637 **Amphetamine toxicity: behavioral and neuropathological indexes.** Federation Proceedings. 34(9):1845-1851, 1975.

An animal model for the assessment of a drug's toxicity is outlined, and findings based on infrahuman studies of amphetamines are reviewed. The model includes behavioral assays, the results of which can be correlated with other functional and morphological changes occuring simultaneously in the experimental organism. Findings do not support the assumption of irreversible pathology after chronic amphetamine use, and indicate that functional deficits evidenced by drug induced behavioral changes disappear with the development of tolerance. Changes in muscle morphology are discussed, and implications for future research are suggested. 43 references.

06 METHODS DEVELOPMENT

213986 Michiels, L. J. M.; Heykants, J. J. P.; Knaeps, A. G.; Janssen, P. A. J. Janssen Pharmaceutica, Research Laboratoria, B-2340, Beerse, Belgium **Radioimmunoassay of the neuroleptic drug pimozide.** Life Sciences (Oxford). 16(6):937-944, 1975.

A radioimmunoassay technique is reported for the quantitative determination of pimozide in which pimozide is made antigenic by coupling it to bovine serum albumin. By using the antiserum, the drug was detected in amounts as low as 50 picogram. The binding capacity of the antibodies was high for pimozide and for the closely related neuroleptic analogs clopimozide, fluspirilene and penfluridol. Therefore, it was concluded that the diphenylbutylamine moiety of the pimozide molecule was required for strong binding. No cross-reaction was observed with the major metabolities of pimozide, even at 500 times higher concentration, so they will not interfere with a radioimmunologic determination of pimozide in human plasma. 15 references. (Author abstract modified)

215655 Roizen, Micheal F.; Weise, Virginia; Moss, Jonathan; Kopin, Irwin J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Plasma catecholamines: arterial-venous differences and the influence of body temperature.** Bethesda, MD, NIMH, 1975. 11 p.

Sensitive radio enzymatic assays were used to measure the influence of body temperature on levels of plasma total catecholamines and norepinephrine in rats, and levels were found to change dramatically with changes in body temperature. The decrease in plasma catecholamines induced by warming the animal is reflected in an apparent arteriovenous difference when arterial blood is obtained at room temperature and tail sampling is aided by heat induced vasodilation. Combined blockade of extraneuronal and neuronal uptake reduces this arteriovenous difference. Blood samples obtained from the decapitated trunk of the rat contain similar levels of plasma catecholamines to those obtained from indwelling carotid catheters. Blood levels of dopamine-beta-hydroxylase were similar whether obtained by venous sampling during heat induced vasodilation, decapitation or indwelling arterial cannula. 11 references. (Author abstract modified)

217219 Karoum, Farouk; Gillin, J. C.; Wyatt, R. J.; Costa, E. Laboratory of Clinical Psychopharmacology, St. Elizabeths Hospital, NIMH, Washington, DC 20032 **Mass-fragmentography of picomole quantities of biogenic amine metabolites in human cerebrospinal fluid as well as whole rat brains. (Unpublished paper).** Bethesda, MD, NIMH, 1975. 14 p.

A mass fragmentographic method is described for the simultaneous assay of both the acidic and alcoholic metabolites of tyramine, octopamine, dopamine and norepinephrine. The method was successfully applied for the measurement of picomole concentrations of these metabolites in human ventricular and lumbar cerebrospinal fluids and in the rat brain. Mass fragmentography was carried out on the methyl ester/pentafluoropropionateproprionate (ME-PFP) derivatives of the acidic and the PFP derivatives of the alcoholic metabolites, employing an eight foot 3% SE 52 column. Chemical methods for the synthesis of a number of deuterated isomers of the above metabolites are also described. These isomers were utilized as internal reference standards for the assay of the metabolites in biological materials and to study the fragmentation reactions of these metabolite derivatives. 10 references. (Author abstract modified)

217528 Teresa A. Silva, M.; Calil, Helena M. Departamento de Psicobiologia, Escola Paulista de Medicina, Rua Botucatu 862, 04023 Sao Paulo, Brasil **Screening hallucinogenic drugs: systemic study of three behavioral tests.** Psychopharmacologia (Berlin). 42(2):163-171, 1975.

The effects of several hallucinogenic and nonhallucinogenic drugs have been studied on three behavioral tests proposed as useful indexes of hallucinogenic activity: heat twitching in mice, defecation in an open-field, and suppression of responding on a differential reinforcement of low rates (DRL) schedule of reinforcement. According to the original propositions, after administration of hallucinogenic agents the frequency of head twitches would increase in mice, the defecation of rats in an open-field would decrease without consistent change in ambulation, rearing and grooming, and the responding of rats on a DRL schedule would yield a typical cumulative record pattern. It was found that the head twitch test was sensitive to mescaline and lysergic acid diethylamide-25 but not to tetrahydrocannabinol or to myristicin and elemicin. Besides, the data on interobserver agreement suggested there is a high degree of subjectivity involved in assessing this response. In the open-field test, nonhallucinogenic drugs such as chlorpromazine and apomorphine fell into the hallucinogenic pattern proposed. In addition, the postinjection interval selected seemed to critically affect defecation scores. The DRL hallucinogenic pattern occurred nonspecifically after administration of hallucinogenic and nonhallucinogenic drugs. It was concluded that the three tests have limited value for screening purposes. 28 references. (Author abstract)

217667 Lehr, Roland E.; Kaul, Pushkar N. Department of Pharmacology, University of Oklahoma, Norman, OK 73069 **Chlorpromazine metabolism IV: quaternization as a key to determination of picomoles of chlorpromazine and other tertiary amine drugs.** Journal of Pharmaceutical Sciences. 64(6):950-953, 1975.

In a study of chlorpromazine metabolism, the reaction of chlorpromazine with 9-bromomethylacridine under appropriate conditions yielded a nonfluorescent quaternary ammonium derivative which, on subsequent photolysis, liberated fluorescence. The major component of this fluorescence was 9-methylacridine (86%), while two minor components were 9-acridinecarboxaldehyde (6%) and 9-acridinemethanol (8%). The mechanism of photolysis leading to formation of these products appeared to involve homolytic as well as heterolytic cleavages of the quaternary salt. Both the quaternization and the photolysis were stoichiometric. Appropriate isolation of the fluorescence and its quantitative determination constituted the basis of a new and highly sensitive assay applicable to chlorpromazine and other tertiary amine drugs. 12 references. (Author abstract)

219631 Lloyd, K. G.; Bartholini, G. Dept. of Psychopharmacology, Clarke Institute of Psychiatry, 250 College St., Toronto, Ontario **The effect of drugs on the release of endogenous catecholamines into the perfusate of discrete brain areas of the cat in vivo.** Experientia (Basel). 31(5):560-562, 1975.

Experiments are reported which demonstrate the usefulness of the push - pull cannula perfusion technique in studying the effects of drugs on the release of picogram quantities of the endogenous catecholamines dopamine and noradrenaline from discrete brain areas. It is noted that the output of catecholamines from various brain regions can also be measured in the unrestrained, unanesthetized cat by means of chronically implanted push - pull cannulae. 18 references.

221273 Lemmingson, Ole; Lullmann, Heinz; Prooter, Harm; de Voss, Reink. Abteilung fur bottnische okologie des nordischen Forschungsrates, Umea, Sweden **/An animal test model for evaluating drugs with anti-mass psychotic activity./** Ein Tiermodell zur Testung anti-massenpsychotisch wirkender Pharmaka. Arzneimittel-Forschung (Aulendorf). 24(1):2070-2073, 1974.

The utility of testing potential anti-mass psychotic drugs using lemmings (Lemmus lemmus) was examined. The conditions for housing and breeding of lemmings are described. Since this species has an inherent tendency to develop a mass psychosis, its behavior is suitable for imitating human mass psychosis and for investigating anti-mass psychotic drugs. Mass psychosis was induced by a drastic reduction of the interanimal distance in a psychosis box. The mass psychotic activities, i.e. the mass migration and the terminal leap into the water, was observed by means of a special device. Preliminary results concerning the influence of some psychotropic drugs upon the model mass psychosis are reported. The findings give rise to expectations that the development of anti-mass psychotic drugs and their testing will be promoted. 8 references. (Journal abstract)

221739 Heidbrink, V.; Mallach, H. J.; Moosmayer, A. Institut fur Gerichtliche Medizin, Universitat Tubingen, Tubingen, Germany **/On the gas chromatographic analysis of benzodiazepines: second communication: diazepam and its metabolites./** Zur gaschromatographischen Analytik der Benzodiazepine: 2. Mitteilung: Diazepam und seine Metabolite. Arzneimittel-Forschung (Aulendorf). 25(4):516-517, 1975.

A gas chromatographic method is reported which completely resolves diazepam and its major metabolites and enables the specific quantitation of these compounds after extraction from serum and urine. The sensitivity limits are about 3 ng/ml if 4 ml serum or urine are extracted. 8 references. (Journal abstract)

222353 Bloom, F. E. Laboratory of Neuropharmacology, Div. of Special Mental Health Research, NIMH, St. Elizabeths Hospital, Washington, DC **Monoaminergic neurotoxins: are they selective? Some perspectives on the symposium held at the Fourth Annual Meeting of the Society for Neuroscience, October, 1974. (Unpublished paper).** Washington, DC, NIMH, 1975, 7 p.

A review of the spectrum of opinions which have evolved concerning the usefulness of 6-hydroxydopamine (6-OHDA) as an experimental tool for neurobiologists is presented. The data

and interpretations of three speakers at the annual meeting of the Society for Neuroscience in 1974 and the published reviews of two other researchers are discussed. The question is asked as to whether intracerebral injections of 6-OHDA can be executed so as to: 1) eliminate the nonspecific damage which will accompany any mechanical penetration of the brain and thereby 2) accomplish within localized zones of the central nervous system the same sorts of selective chemical sympathectomy achieved by parenteral doses of 6-OHDA. It is concluded that 6-OHDA can provide useful chemical denervation restricted to the central catecholamine neurons when properly administered, provided that each injection is fully evaluated by biochemical, cytochemical and physiological indices. 7 references.

222802 Kawashima, Koichiro; Dixon, Ross; Spector, Sydney. Department of Physiological Chemistry, Roche Institute of Molecular Biology, Nutley, NJ 07110 **Development of radioimmunoassay for chlorpromazine.** European Journal of Pharmacology (Amsterdam). 32(2):195-202, 1975.

The development of radioimmunoassay for chlorpromazine is described. Antiserum against chlorpromazine (CPZ) was produced in rabbits immunized with CPZ haptene conjugated to bovine serum albumin. The antiserum was used to develop a radioimmunoassay for CPZ. As little as 10pg of CPZ can be detected with this radioimmunoassay. Although the antibody can bind 7-HO-CPZ, 8-HO-CPZ and promazine, the concentrations required to produce a 50% inhibition of 3H-CPZ-antibody binding are 5-10 times greater than CPZ. The plasma levels of CPZ and some minor metabolites in rats following administration of 10mg/kg i.v. were determined by radioimmunoassay and showed a biphasic decay curve. Brain levels revealed that following i.v. administration CPZ traverses the blood - brain barrier rapidly and achieves peak concentration within 5 min. Plasma and brain levels can be detected for at least 24 hr. 18 references. (Author abstract modified)

222829 Jain, Naresh C.; Budd, Robert D.; Sneath, Thomas C. Rancho Los Amigos Hospital, 7601 E. Imperial Highway, Downey, CA 90242 **Rapid mass screening and confirmation of urinary amphetamine and methamphetamine by gas chromatography.** Clinical Toxicology. 8(2):211-224, 1975.

A rapid and simple procedure is described for the mass screening and confirmation of amphetamine and methamphetamine in urine using gas chromatography with flame ionization detector. The amphetamine drugs are screened as free drugs on a 10% Apiezon L-10% KOH column and confirmed as their trifluoroacetamide derivatives on a 3% OV-17 column. This dual approach eliminates false positives and interfering substances that may be present in the urine and is, therefore, specific for amphetamine and methamphetamine. 33 references. (Author abstract modified)

222830 Wu, Anthony. Department of Environmental Medicine, Medical College of Wisconsin, Milawulkee, WI **Rapid analysis of the central nervous system stimulants, amphetamines, via gas chromatography-mass spectrometry: rapid acylation in the presence of a mercury catalyst.** Clinical Toxicology. 8(2):225-232, 1975.

A simple, direct, instantaneous, and quantitative acetylating procedure for amphetamines is described. The method uses trifluoroacetic anhydride in the presence of mercuric trifluoroacetate as a catalyst. The product was characterized by a gas chromatography mass spectrometry system. The salient features of this technique are: (a) rapidity of analysis; (b) no previous cleanup to remove adulterants; and (c) detection of amphetamines at the picomole level. It is noted that the method could prove to be applicable, with minimum amounts of involvement in sample preparation, to the analysis of a variety of compounds containing an acyl displaceable hydrogen. 4 references. (Author abstract)

225168 Morse, W. H. Department of Psychiatry, Harvard Medical School, Boston, MA 02115 **Schedule-controlled behaviors as determinants of drug response.** Federation Proceedings. 34(9):1868-1869, 1975.

The use of schedule contingencies as analytical tools in investigating specific topics in behavioral pharmacology is discussed. Schedule controlled performances began to be used in assessing the behavioral effects of drugs because of practical advantages over other techniques for studying behavior. Schedule controlled behavior is, however, of fundamental importance in behavioral pharmacology. It has been found repeatedly that the effects of many drugs depend critically upon the patterns of responding engendered by different schedule contingencies. These dependencies of the effects of drugs on schedule controlled behavior occur because ongoing behavior is itself an important determinant of drug action. 2 references. (Author abstract modified)

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

213387 Bartlett, P.; Forrest, A. Royal Edinburgh Hospital, Edinburgh, Scotland **Evaluation of benapryzine in psychotic patients treated with phenothiazines.** Current Medical Research Opinion. 2:313-318, 1974.

The efficacy of benapryzine for the control of parkinsonian symptoms induced by phenothiazines was assessed in 23 patients, 20 male and 3 female, ranging in age from 15 to 69 years, 19 of whom had been diagnosed as schizophrenic. Findings indicate that 21 of the 23 patients were free from parkinsonian signs and symptoms during the prebenapryzine week, and 19 remained completely symptom and sign free during the benapryzine treatment weeks. Assessments of functional capacity and general behavior indicated that 20 patients showed no improvement of their functional capacity at any time. Eleven patients were completely free from side-effects throughout the trial. It is concluded that benapryzine appears to be an effective remedy for drug induced parkinsonism and one which generates few side-effects. 17 references.

213596 Saito, Masami. Department of Psychiatry and Neurology, Kansai Medical School, Osaka, Japan **New psychotropic drug research in Japan.** Psychopharmacology Bulletin. 11(2):15-19, 1975.

Actual conditions of new psychotropic drug research in Japan are described. Three aspects are emphasized: the procedures for conducting research with new drugs on patients; several interesting new drugs developed in Japan; and some peculiarities of clinical drug treatments in Japan. There is still deep rooted opposition to the use of patients for research with new drugs developed outside Japan. 9 references.

213598 Herrmann, W. M. Schering AG, Klinische Forschung, Neuropsychopharmakologie, Berlin, Germany **New psychotropic drug developments in the USSR and other Eastern European countries.** Psychopharmacology Bulletin. 11(2):24-28, 1975.

The development of new psychotropic drugs in Eastern European countries and the USSR is discussed, emphasizing that research has led to almost identical limitations of the known psychotropics. One Czechoslovak group and one Moscow group have been developing new psychotropic substances. The Czech group has apparently been successful in dissociating the hallucinogenic and other psychotropic, particularly stimulatory, effects of LSD. In Moscow, small molecules are being developed similar to serotonin; new tricyclic and tetracyclic psychotropics are also being developed. Another program involves mesoionic compounds, the sydnones and sydnonimines. Clinical trials using sydnocarb in mixed patient groups are reported. 13 references.

215073 Haskovec, L.; Jirsak, R.; Srutova, K. Department of Psychiatry, Charles University, Praha 2, Ke Karlovu 11, Czechoslovakia **Encephabol in patients with organic brain-syndrome.** Activitas Nervosa Superior (Praha). 16(4):259-260, 1974.

At the 16th Annual Psychopharmacological Meeting, Jesenik, 1974, a paper was presented in which the effect of Encephabol on 24 patients with an organic brain syndrome was examined in a double blind cross over research design with each patient serving as his own control. Twenty three patients scored better on Encephabol than on placebo, with nine patients showing an unequivocal improvement. The improvements were shown in terms of higher energy level, broadening of interests, and improvement of the thinking process. Symptoms were also improved, including fatigue, speed of thinking, nervousness, depression, perception, and heart discomfort. Three tests measuring memory retention, concentration, flexibility and speed of the thinking process were used for psychological examination. A significant improvement of the memory retention test in the Encephabol treated patients were noted. No severe side-effects were noticed. 1 reference.

220858 Perris, Carlo. Department of Psychiatry, Umea University, Umea, Sweden **A multicenter multidimensional study of some new longacting neuroleptic drugs.** Acta Psychiatrica Scandinavica (Supplement) (Kobenhavn). Supplement 249:1-134, 1974.

The scale devised by Martens and Jonsson for use with chronic schizophrenic patients was analyzed using factor analytic techniques. The analytic program required that Eigenvalues should not be below 1.00. Six main factors were obtained. The data from previous controlled trials of fluspirilene versus fluphenazine enanthate and of pimozide versus trifluoperazine have been reanalyzed so as to show the possible effects of these drugs on the different factors. In neither of te two trials was any difference found between the drugs. Fluspiriline and fluphenazine enanthate show a significant effect on factor II which comprises items descriptive of what may be considered a passive, retarded, autistic syndrome. Pimozide and trifluoperazine show a significant effect on the same factor as well as on factor I which contains some items indicative of affective disturbances and hostility together with a second component comprising paranoid ideas, splitting and blocking. 22 references. (Author abstract modified)

08 DRUG TRIALS IN SCHIZOPHRENIA

213527 Meltzer, H. Y.; Sachar, E. J.; Frantz, A. G. Department of Psychiatry, University of Chicago Pritzker School of Medicine, Chicago IL **Dopamine antagonism by thioridazine in schizophrenia.** Biological Psychiatry. 10(1):53-57, 1975.

The theory that thioridazine is clinically as effective a treatment of schizophrenia as other neuroleptic drugs but appears to have much less dopamine blocking properties than these agents in man and laboratory animals was examined. Serum prolactin levels are increased by dopamine receptor blocking drugs. It was found that thioridazine is as effective as chlorpromazine, trifluperazine, and prolixin enanthate in increasing serum prolactin levels in unmediated schizophrenic patients, indicating it is an effective dopamine blocking agent. 23 references. (Author abstract modified)

213530 Jus, A.; Jus, K.; Villeneuve, A.; Gautier, J.; Pires, P.; Lachance, R.; Villeneuve, R. Research Department, Hopital St. Michel-Archange, Quebec, Canada **Influence of reserpine on all-night sleep pattern in nonlobotomized and lobotomized chronic schizophrenic patients.** Biological Psychiatry. 10(1):17-25, 1975.

The influence of reserpine on all night sleep pattern in nonlobotomized and lobotomized chronic schizophrenic patients was examined. The groups were matched for age, sex, duration of illness, clinical symptoms, type and dose of

psychopharmacological treatment. The patients of both groups were administered 1mg of reserpine half an hour before bedtime, for 3 successive days. Before reserpine administration the mean percentage time of the non-rapid eye movement (NREM) stage 4 was significantly higher in the lobotomized group. There was no significant difference in the REM parameters. After 3 days of reserpine administration in the nonlobotomized group, there was no significant difference in the mean percentage of the NREM stage 4, whereas the mean REM percentage significantly increased and REM latency decreased. In the lobotomized group the same procedure, i.e. 3 days of reserpine administration, provoked a significant decrease in the mean percentage of the NREM stage 4 and no significant changes in the REM parameters. This difference in reserpine action on sleep in the lobotomized group is discussed. 27 references. (Author abstract modified)

213623 Pfeiffer, Carl C. New Jersey Mental Health Research and Development Fund, Skillman, NJ **Cerebral neurohumors and behavior.** Psychopharmacology Bulletin. 11(2):55-56, 1975.

Biochemical disorders that may underlie schizophrenia are being studied. Disorders in the metabolism of biogenic amines and the effect of methylated compounds on central nervous system stimulatory activity are being explored. In animal studies, changes in electrical activity of the brain are examined after administration of methylated and nonmethylated stimulants; the effects of these stimulants on the acetylcholine and amine content of specific portions of the brain are then determined. In human subjects, both normal and schizophrenic, changes in blood levels of biogenic amines and EEG changes after administration of various drugs are measured. It is theorized that some schizophrenic states may result from chemically induced overstimulation of the brain. A probable etiological factor is a combined deficiency of zinc and manganese with a relative increase in iron or copper or both. Significant relationships have been found between histamine level and changes in psychiatric ratings.

213704 Wyatt, Richard Jed. NIMH Laboratory of Clinical Psychopharmacology, William A. White Bldg., St. Elizabeths Hospital, Washington, DC 20032 **/Comment on Linus Pauling's theory of orthomolecular psychiatry./** Comment. American Journal of Psychiatry. 131(11):1258-1262, 1974.

The findings of a possible genetically determined deficiency in platelet monoamine oxidase in some schizophrenics and the finding that some chronic patients respond to a massive dose of the serotonin precursor 5-hydroxytrytophan compared with placebo are discussed. The scientific justification for the claims made by megavitamin therapists are examined. It is concluded that, while the concepts of orthomolecular psychiatry are attractive and stimulating, the data supporting them are weak, and therapeutic claims based upon them are unwarranted. 25 references.

213726 Singh, Man Mohan; Kay, Stanley R. Clinical Psychopharmacology Service, Bronx Psychiatric Center, 1500 Waters Place, Bronx, NY 10461 **Therapeutic reversal with benztropine in schizophrenics: practical and theoretical significance.** Journal of Nervous and Mental Disease. 160(4):258-266, 1975.

The effect of an anticholinergic antiparkinsonism drug, benztropine, on the therapeutic course of neuroleptic treatment in 18 schizophrenics was investigated in a double-blind crossover study involving haloperidol and chlorpromazine. Significant therapeutic reversal was observed with benztropine in terms of the social, affective, cognitive dysfunctions characteristically seen in schizophrenic psychosis. The effect was one of exacerbation of the disorder and not a toxic confusional state sometimes associated with anticholinergic drugs. It is suggested that the benztropine reversal of therapeutic changes supports the hypothesis that cholinergic neuronal mechanisms are involved in schizophrenic decompensation and its restitution with neuroleptics. 17 references. (Author abstract modified)

213764 Rappaport, Maurice; Hopkins, H. Kenneth; Hall, Karyl; Belleza, Teodoro; Hall, Robert A. Research Dept., Agnews State Hospital, San Jose, CA 95114 **Schizophrenia and evoked potentials: maximum amplitude, frequency of peaks, variability, and phenothiazine effects.** Psychophysiology. 12(2):196-207, 1975.

Averaged visual evoked potentials (AVEPs) in normal subjects and in schizophrenics off and on phenothiazine medication were compared. Flashes of four intensities were used. Ss were tested three times within a 1 month period. Measures of maximum amplitude (Am), frequency of peaks, (FOP), and variability (V) were obtained. With increases in stimulus intensity all Ss showed increases in Ams and decreases in FOPs and V. Schizophrenics had smaller Ams, greater FOPs, and greater V than normals. Schizophrenics on phenothiazines generally had less FOPs initially and after 1 wk on medication but not after about 1 month on medication. There was no consistently significant effect of phenothiazines on maximum amplitude. No drug effect on variability was observed. Schizophrenics showed a decrease in FOPs over time while normals showed an increase. A relationship was found between variability and overall thought disturbance. Changes in clinical condition over a month were not associated with discernible AVEP changes. Relationships between Am, FOP, and V are presented. 35 references. (Author abstract)

213863 Itil, T. M.; Marasa, J.; Saletu, B.; Davis, S.; Mucciardi, A. N. 150 White Plains Road, Tarrytown, NY 10591 **Computerized EEG: predictor of outcome in schizophrenia.** Journal of Nervous and Mental Disease. 160(3):188-203, 1975.

Correlations between psychopathological alterations and computer analyzed electroencephalogram (EEG) changes were examined and the predictive value of computerized EEG in the outcome of drug treatment of schizophrenia was studied in a double blind crossover study. The neuroleptics used in the study were fluphenazine, thiothixene, and haloperidol. It was determined that schizophrenic patients who have more high frequency fast activity and a lesser degree of alpha and slow waves in computerized EEG before the treatment have a better therapeutic outcome to the major tranquilizer treatment. The correlation between pretreatment high frequency computer EEG measurements and better therapeutic outcome was statistically significant. Therapy resistant schizophrenic patients were characterized by a lesser degree of very fast beta activity, more alpha waves and slow waves, higher amplitudes in computer EEG, and a lesser degree of acute psychotic symptomatology but more negative symptoms such as motor retardation and blunted affect. Schizophrenic patients with certain psychopathological profiles had similar computer EEG profiles. 39 references. (Author abstract modified)

215075 Remr, J.; Nekolova, J.; Heinzl, Z. Psychiatric Department, 460 63 Liberec, U.S.S.R. **A comparison of the therapeutic effect of oxypertine and thioridazine in chronic schizophrenia (a controlled trial).** Activitas Nervosa Superior (Praha). 16(4):261-262, 1974.

At the 16th Annual Psychopharmacological Meeting, Jesenik, 1974, a paper was presented in which the therapeutic effect of oxypertine and thioridazine in 34 chronic schizophrenic patients aged 32 to 60 was described. The state of the patients after both compounds was approximately the same; oxypertine was not less effective than thioridazine and in affectivity it was superior. Because of its different chemical structure, its use is advisable in cases in which phenothiazines are contraindicated for somatic reasons. 10 references.

215456 Quitkin, Frederic; Rifkin, Arthur; Kaplan, Joel H.; Klein, Donald F. Department of Psychiatry, Long Island Jewish-Hillside Medical Center, Glen Oaks, NY **Treatment of acute schizophrenia with ultra-high-dose fluphenazine: a failure at shortening time on a crisis-intervention unit.** Comprehensive Psychiatry. 16(3):279-283, 1975.

The efficacy of a 100mg to 1200mg per day fluphenazine regimen was tested in acute schizophrenic patients in the hope of speeding remission. Ten patients were treated in an open study with the ultra high dose regimen. Patients were considered to have good to excellent response if within 4 weeks they were virtually free of psychotic symptoms and had achieved reconstitution. A fair response consisted of a marked diminution of psychotic symptoms at 4 weeks, which were nevertheless still obvious on mental status examination. Patients who had little or no improvement were considered to have had poor responses. Five patients had good to excellent responses, one was fair, and four had poor responses. These results are no better than those achieved with the standard, vigorous, combined intramuscular and oral chlorpromazine treatment. It is concluded that high dose fluphenazine did not produce quicker remissions nor increase the percentage of patients showing marked improvement. 8 references.

215701 Jus, K.; Beland, C.; Bouchard, M.; Jus, A.; Fontaine, P.; Brunelle, R. Research Division, Hopital St. Muche-Archange, Quebec 5, Canada **Polygraphic night sleep pattern during chronic single and multiple neuroleptic dose administration.** International Pharmacopsychiatry (Basel). 10(1):58-63, 1975.

A comparison was made between the polygraphic night sleep pattern of chronic schizophrenic patients who were receiving a single dose of neuroleptics at bedtime and between the night sleep pattern of the same patients receiving the same amount of the same neuroleptic divided into 3-4 doses during daytime. It was shown that the single bedtime dose provoked a significant increase in the mean percentage of nonrapid eye movement stage 4 and of the mean percentage of the REM state whereas the mean percentage of the NREM stage 2 was significantly decreased. 16 references. (Author abstract)

216188 Gallant, D. M.; Mielke, D.; Bishop, G.; Oelsner, T.; Guerrero-Gifueroa, R. Dept. of Psychiatry and Neurology, Tulane University School of Medicine, New Orleans, LA 70112 **Pipotiazine palmitate: an evaluation of a new long acting intramuscular antipsychotic agent in severely ill schizophrenic patients.** Diseases of the Nervous System. 36(4):193-196, 1975.

A new long-lasting antipsychotic agent, pipotiazine palmitate, was studied. Findings support earlier investigations in attesting to the antipsychotic efficacy and relatively low toxicity when used in the treatment of severely ill schizophrenic patients. It is noted that this particularly long-acting antipsychotic preparation appears to have an even longer duration of activity than some of the other available standard long-lasting agents. It is suggested that the availability of this type of preparation is not only economical in terms of nursing care and hospital cost but should also increase the efficacy of psychopharmacologic treatment of schizophrenics by reducing both patient errors and staff errors in administration of medication. It is noted that the clinical disadvantages of pipotiazine palmitate is the delay in onset of therapeutic activity after injection, since significant improvement is noted after 3 to 4 days. Other implications of recent research are discussed. 4 references.

216190 Meadow, Arnold; Donlon, Patrick T.; Blacker, Kay H. Department of Psychiatry, School of Medicine, University of California, Davis, CA **Effects of phenothiazines on anxiety and cognition in schizophrenia.** Diseases of the Nervous System. 36(4):203-208, 1975.

The effects of phenothiazine drugs on anxiety and conceptual disorganization in schizophrenia were investigated with two groups of patients. The first group was studied during a period of abrupt medication withdrawal with secondary psychotic decompensation and the second group during a period of psychic reintegration on active medication. Findings reveal that, for the drug withdrawal group, discontinuation of phenothiazines produced a statistically significant increment on both measures of anxiety. Results with respect to cognitive disorganization are more equivocal. Findings indicate that with the withdrawal of medication there is a significant increment on the ratings of cognitive disorganization but no significant difference in the "looseness of association" measure. In the hospital group, when the patients were placed on phenothiazines, anxiety was not significantly affected on both measures, but conceptual organization was significantly decreased. 11 references.

216403 Frost, Monica. no address **Schizophrenia -- 5: physical treatments and drugs.** Nursing Times (London). 71(13):506-507, 1975.

Some of the physical treatments and drugs used for the treatment of schizophrenia since the 1930s are reviewed. Emphasis is on electroconvulsive therapy, deep insulin coma treatment, modified insulin treatment, psychotherapy, and drug therapy. Currently used drugs which are considered include tranquilizers, such as chlorpromazine, Modecate, Depixol, phenothiazines and allied drugs. The use of anti-Parkinson drugs to counteract the side-effects of the phenothiazines is also noted. 5 references.

216759 Dufour, H.; Castelli, J.; Luccioni, H.; Scotto, J.-C.; Sutter, J.-M. Clinique Universitaire de Psychiatrie de la Faculte de Medecine de Marseille, France /**A new substituted benzamide with neuroleptic effects: Lin. 14 18 or sultopride.**/ Une nouvelle benzamide substituee a effets neuroleptiques: Le Lin. 14 18 ou sultopride. Encephale (Paris). 1(1):15-18, 1975.

At the Ninth Congress of the International College of Neuro-psychopharmacology, Paris, July 1974, a paper was presented in which a new benzamide, sultopride (LIN. 14 18), was investigated in treating maniacal states of agitation and schizophrenia. Normalization or important improvement was observed in 11 cases, slight improvement in 9, and 2 cases became worse. Sultopride was well tolerated, although the extrapyramidal side-effects characteristic of neuroleptics were observed in 25 patients. It is concluded that: the psychotropic effects of the drug are powerful and regular; the prevailing action is both antipsychotic and disinhibiting; while all chronic and acute psychoses seem to respond to the drug, the quality of the results obtained with chronic psychoses, especially schizophrenia, are particularly striking. (Author abstract modified)

217025 Perales C., J. Alberto; Garcia M., Albeto; Infantes P., Victor; Valle E. D.; Godofredo. Av. Arequipa 2053, Lima, Peru **/Comparative study of clotiapine and trifluoperazine in episodes of acute paranoid schizophrenia./** Estudio comparativo de la clotiapina y de la trifluoperazina en episodios agudos de esquizofrenia paranoide. Acta Psiquiatrica y psicologica de America latina (Buenos Aires). 20(3):207-213, 1974.

A new drug, clotiapine, was used in a comparative study (controlled, double-blind) with trifluoperazine, in equivalent doses, in the treatment of acute paranoid schizophrenia. Thirty patients were studied in two groups of 15, each of which received one of the drugs. Therapeutic and secondary effects were assessed, with special attention to extrapyramidal side-effects by means of standard scales and clinical procedures. Results suggest that clotiapine is preferable, specifically with regard to the following symptoms: hostility, paranoid mood and thought, estrangement, hallucinatory syndromes and emotional isolation. There was a lower incidence of Parkinsonism. However, these clinical results had no statistical significance. 17 references. (Journal abstract modified)

217154 Charalampous, K. D.; Johnson, Philip C.; Estevez, Vincent. Dept. of Psychiatry, Baylor College of Medicine, Houston, TX 77025 **Absorption and excretion of thioridazine and mesoridazine in man.** Diseases of the Nervous System. 35(11):494-496, 1974.

Tritium labeled thioridazine and mesoridazine were given to four schizophrenic subjects to determine if differences in reported clinical potency of these two drugs could be explained by different rates of absorption and excretion. Mesoridazine was found to have earlier peak levels and lower fecal excretion. However, the blood and fecal differences were too small to be an adequate explanation for the differences in clinical potency, suggesting that the rate of metabolic degradation is a more likely explanation for the potency difference. 10 references. (Author abstract modified)

217454 Rappaport, M.; Hopkins, H. K.; Hall, K.; Belleza, T. Research Department, Agnews State Hospital, San Jose, CA 95114 **Phenothiazine effects on cerebral-evoked potentials and eye movements in acute schizophrenics.** International Pharmacopsychiatry (Basel). 10(2):111-124, 1975.

The effects of phenothiazine on averaged visual evoked potentials (AVEP) and on eye movements in hospitalized, young, acute schizophrenic patients were examined. These results were compared with those of normal subjects who were not given medication. AVEP measures included maximum amplitude (Am), frequency of peaks (FOPs), variability (V) and peak latencies for an early negative peak (N1) and a later positive peak (P6). Eye movement measures included percent of time looking at a stimulus slide, percent of time looking at a figure on the slide, the number of fixations and the percent of cells entered in which fixations occurred. For schizophrenics off and on phenothiazine medication, there were no consistently significant drug effects on any measure except frequency of peaks. Schizophrenics compared to normals had lower amplitudes, greater frequency of peaks, greater variability and lower eye movement scores. 5 references. (Author abstract)

217810 Clark, Mervin L.; Paredes, Alfonso; Costiloe; J. Paul; Wood, Fredda; Barrett, Agnes. Department of Medicine, University of Oklahoma Health Sciences Center, Norman, OK **Loxapine in newly admitted chronic schizophrenic patients.** Journal of Clinical Pharmacology. 15(4, Part 1):286-294, 1975.

The efficacy of loxapine (LOX) in newly admitted acutely exacerbated chronic schizophrenic patients was examined. Only 8% of the patients receiving placebo improved to any degree compared to 58% to 67% improvement for trifluoperazine (Stelazine) and loxapine. The standard drug Stelazine at a dose of 50mg/day exhibited therapeutic activity significantly different from placebo activity on several variables. Loxapine in doses of 100mg/day could be differentiated from placebo on only one variable and one item in the Brief Psychiatric Rating Scale. 17 references.

218213 Klawans, Harold L., Jr.; Westheimer, Ruth; Goetz, Christopher C. Dept. of Neurology, Michael Reese Hospital, Chicago, IL **A pharmacological model of the pathophysiology of schizophrenia.** Diseases of the Nervous System. 36(5):267-275, 1975.

A pharmacological model of the pathophysiology of schizophrenia based upon receptor site theory is presented. The model proposes that, like any neuronal function, schizophrenia is triggered by the action of a small molecule at a specific receptor site. This model permits analysis of all existing theories of the pathogenesis of schizophrenia and makes it possible to view the pathophysiological implications of these theories. It also makes it possible to understand the mechanism of action of neuroleptic agents used in the treatment of schizophrenia, regardless of which theories of pathogenesis are valid. 65 references. (Author abstract modified)

218254 Frederiksen, P. K. Lillhagens Sjukhus, 422 03 Hisings Backa 3, Sweden **Baclofen in the treatment of schizophrenia.** Lancet (London). 1(7908):702-703, 1975.

The effect of baclofen in 13 schizophrenic patients is discussed, based on the hypothesis that schizophrenia is caused by lack of an inhibiting factor. Progressive return to normal associative functions and reintegration of personality was observed. Improvements were found in autism and hallucinations, often within a few days. The intensity of symptoms, such as rigidity or depressed function, was decreased as previously instituted phenothiazine treatment was reduced.

219536 Brown, W. T. no address **Megavitamin and orthomolecular therapy of schizophrenia.** Canadian Psychiatric Association Journal (Ottawa). 20(2):97-100, 1975.

The literature on megavitamin and orthomolecular therapy of schizophrenia is reviewed, and the controversy between practitioners of conventional and orthomolecular psychiatry is outlined. The following statements are offered as a basis for discussion between the opposing camps: 1) nicotinic acid or nicotinamide, when used as an adjunct to conventional therapies such as barbiturates and electroconvulsive treatment, may have a beneficial effect in the treatment of some patients suffering from acute, early schizophrenia; 2) megavitamin therapy has not been demonstrated to be generally efficacious in the treatment of the vast majority of chronic schizophrenic patients; 3) or orthomolecular psychiatry are defined by Linus Pauling has now superseded megavitamin therapy; 4) methodological problems are enormous; 5) Schizophrenics Anonymous and similar self-help groups which are outgrowths of orthomolecular psychiatry, and which serve to reduce loneliness, shame and guilt, have useful psychological and social value. It is concluded that orthomolecular psychiatrists should be given audience in conventional psychiatric journals.

219537 Ban, Thomas A.; Lehmann, Heinz E. Department of Psychiatry, McGill University, Montreal, Quebec **Nicotinic**

acid in the treatment of schizophrenias: Canadian Mental Health Association Collaborative Study Progress Report II. Canadian Psychiatric Association Journal (Ottawa). 20(2):103-112, 1975.

Clinical trials in the Canadian Mental Health Association (CMHA) collaborative study of nicotinic acid in the treatment of schizophrenias are reported. Two general hypotheses are tested: that nicotinic acid has a beneficial effect in schizophrenic patients over and above the effect achievable by standard treatment; and that prior and simultaneous administration of nicotinic acid can prevent the exacerbation of psychopathology in schizophrenic patients when it would be induced by the combined administration of a monoamine oxidase inhibitor (tranylcypromine) and a methyl donor (methionine), and that nicotinic acid can attenuate or improve the psychopathology thus induced. Results indicate that nicotinic acid had no effect, or had a negative therapeutic effect, in both newly admitted and chronic schizophrenic patients. 25 references.

220156 Nishiura, Masanaka. Keihan Hospital, Japan **Clinical study of haloperidol. I. Techniques and theory of parenteral therapy.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(7):759-771, 1974.

The effect of haloperidol in 80 schizophrenic patients exhibiting hallucination, delusion, anxiety, irritation and psychomotor excitation was studied. Ss were intramuscularly (i.m.)or intravenously treated with this drug (15-60 mg/day) for 3-18 days. Haloperidol was effective in 88.8% of the patients, and was most effective with a dose of 30-60mg/d . The effects appeared 2 days after the injection. Extrapyramidal symptoms were observed most frequently in those treated with a small i.m. dose of 15-20mg/day, less frequently in those treated with a larger i.m. dose than 30mg/day, and were not observed at all among those treated intravenously. This drug was most effective on hallucination, delusion, anxiety, irritation and excitation. 20 references.

220267 Gonzalez Lopez, J. L. no address **/Monoclorimipramine in schizophrenia./** La monoclorimipramina en la esquizofrenia. Revista de Psiquiatria y Psicologia Medica (Barcelona). 11(5):315-320, 1974.

Monoclorimipramine (Anafranil) was tested in 22 schizophrenics of varying ages and both sexes who were intravenously injected with the drug. Best effects were obtained in hebephrenic - catatonic forms, hyposynthetic catatonics, depressed schizophrenic states and particularly in schizophrenic defects based upon adaptation - dependency problems in familial and social life. Side-effects were insignificant. 10 references.

220425 Temkov, I. no address **/Psychopharmacological principles of rehabilitationg mental patients./** Psikhofarmakologicheskiye predposylki reabilitatsii psikhicheski bol'nykh. In: Kabanov, M., IV Mezhdunar. Simpoz. po Reabilit. Psikhicheski Bol'nykh. Leningrad, Psikhonevrologicheskiy Institut, 1974. 331 p. (p. 207-209).

In a paper presented at the Fourth International Symposium on Rehabilitation of the Mentally Ill held in Leningrad, October 1974, the psychopharmacological treatment of schizophrenic patients in combination with social and psychological therapy was examined. Special attention must be given to the creation of a favorable home and work environment. It is concluded that drug therapy is especially effective in the rehabilitation of chronic schizophrenics. (Journal abstract modified)

221338 Tacke, B.; Freistein, H.; Kempf, H.; Windheuser, A. Rheinisches Landeskrankenhaus Psychiatrische Universitatsklinik, 4 Dusseldorf 12, Bergische Landstrasse 2 **/Pilot study of 2-pyrrolidon acetamide (generic name: piracetam)./** Klinische Prufung von 2-Pyrrolidon-Acetamid (Generic Name: Piracetam) -- Eine Pilot Study. Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 8(2):82-89, 1975.

Ten chronic schizophrenics were tested by clinical observations, psychological tests and ratings with the Wittenborn Psychiatric Rating Scales before and after taking 2-pyrrolidon acetamide. The improvement in obstructive behavior, apathy, withdrawal and affective flatness in seven patients justifies a double-blind psychometric evaluation concerning the effect of Piracetam on the schizophrenic deficiency states. 17 references. (Journal abstract)

221558 Kampman, Reima; Hirvenoja, Reijo. OYKS:n Psykiatrian Klinikka, 902 10 Oulu 21, Finland **/Perphenazine enanthate in treating chronic schizophrenia./** Perfenazin enantat vid varden av kronisk schizofreni. Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(4):221-226, 1974.

Nineteen hospitalized schizophrenic patients were given a perphenazine enantate injection, 100mg i.m.,once a fortnight for 4 weeks, and 19 patients were given perphenazine tablets, 8mg three times a day, for 4 weeks. The effects of these two kinds of treatment were compared according to the double-blind principle. The perphenazine injection proved to be therapeutically better than tablets, but it had more harmful side-effects. No changes were observed in the laboratory tests. 9 references. (Author abstract modified)

221635 Rasmussen, S.; Haastrup, S.; Kirk, Lars. no address **/Lithium treatment of schizophrenia: a controlled experiment./** Litium-behandling af skizofrene: en ka trolleret undersogelse. Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(6):457-458, 1974.

Lithium treatment in schizophrenia was studied in 15 female patients averaging age 59, with illnesses of average 33 years duration. None were schizoaffective, and 13 were lobotomized. The study lasted 24 weeks, with a 6 week placebo period. Irritability and demand for p.n. (full requirement) medicine increased in the placebo period, but the increase was not statistically significant. A positive correlation between increased irritability and use of p.n. medication was found. The experimental design which permitted p.n. medication may have masked lithium's effect on irritability. The study should have found the same results as Nurses' Observation Scale for Inpatient Evaluation (NOSIE-30): contact and well-being significantly increasing and aggression diminishing. The difference in the above study was not significant, however, and only 7 of the 15 patients benefited from the lithium treatment. 4 references.

221636 Ahlfors, Ulf Goran. Malmakersvagen 8 c 21, SF-00300 Helsingfors, Sweden **/Cross-analysis of a controlled experiment with pipothiazine and fluphenazine enanthate./** Tvaranalys av ett kontrollerat forsok med pipotiazinundecylenat och flufenazinenantat. Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(6):459-461, 1974.

A cross-analysis of a pilot study and a double-blind experiment of the effect of pipothiazine and fluphenazine enanthate on schizophrenic symptoms is presented in three graphs based on the Brief Psychiatric Rating Scale (BPRS). BPRS marks 16 qualitative symptom points and has a 7 point scale for symptom severity. In an 8 week study comparing pipothiazine and

fluphenazine enanthate, the two drugs were found to have equal therapeutic value in improving total schizophrenic symptoms, but each accented different symptoms. A divergence of over 30% was found in relief of guilt, tension, mannerisms, aggression, hallucinations, and atypical symptoms. Pipothiazine seemed slightly more effective, but the difference was not significant. 1 reference.

221637 Gerlach, Jes; Munkvard, I. S:t. Hans Hospital, afd. C, DK-4000 Roskilde, Denmark **/Clozapine and haloperidol: clinical and biochemical aspects in the treatment of schizophrenia./** Clozapin og haloperidol: kliniske og biokemiske aspekter i skizofrenibehandlingen. Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(6):463, 1974.

In a controlled study with 20 schizophrenic patients, clozapine (Leponex) and haloperidol significantly reduced the intensity of schizophrenic symptoms. Clozapine, a diabenzodiazepine derivative with antipsychotic qualities, was significantly better than haloperidol in the treatment of somatic anxiety, fear, stress, mental unrest, bizarre motor activity, and other factors measured by the Brief Psychiatric Rating Scale. The difference was most marked in cases of psychomotor unrest, agitation, and aggression. Side-effects of clozapine include sedation, hypersalivation, and initial orthostatic blood pressure decrease.

221822 Angst, J.; Woggon, B. Psychiatrische Universitatsklinik, Forschungsdirektion, Postfach 68, CH-8029 Zurich, Switzerland **/Clinical study of five depot neuroleptics, comparison of activity profiles of fluphenazindecanoate, fluspirilene, penfluridol, perphenazine-enanthate and pipothiazinepalmitate./** Klinische Prufung von funf Depotneuroleptika: Vergleich der Wirkungsprofile von Fluphenazindecanoat, Fluspirilen, Penfluridol, Perphenazinoenanthat und Pipothiazinpalmitat. Arzneimittel-Forschung (Aulendorf). 25(2):267-270, 1975.

Five depot neuroleptics (fluphenazine decanoate, fluspirilene, pipothiazinepalmitate, penfluridol and perphenazine-enanthate) were compared based on clinical trials in subacute and chronic schizophrenic patients. The psychopathological symptoms were documented by means of the AMP system. Statistical analyses show several differences between the effects of the five substances. The AMP system proved a useful instrument to differentiate similar drugs. 8 references. (Journal abstract)

221989 Niskanen, Pekka; Achte, Kalle; Jaskari, Martti; Karesoja Matti; Melsted, Bogi; Nilsson, Lars Bertil. no address **Results of a comparative double-blind study with clozapine and chlorpromazine in the treatment of schizophrenic patients.** In: Psychiatria Fennica. Helsinki, Helsinki Univ. Central Hosp., 1974. 408 p. (p. 307-313).

The effects of clozapine were compared with those of chlorpromazine in the treatment of schizophrenia in a 40 day double-blind study. Tolerance and side-effects such as tiredness or dizziness were assessed for 48 schizophrenic patients of both sexes who were selected from three Finnish hospitals. Three detailed graphs illustrate the improvement in symptoms during treatment of both experimental groups according to Brief Psychiatric Rating Scale factors. Some of the details gleaned from results of the somatic examination and laboratory tests are discusssed. The clozapine group had improved twice as much by the twentieth day in regard to tension, aggression, excitement, and other symptoms of schizophrenia. A rise in body temperature in this group was also noted. 37 references. (Author abstract modified)

222158 Kaji, Shizuo; Tsukada, Koji; Hasegawa, Seiichi; Yamaguchi, Shozo; Terai, Taku; Tanaka, Masaharu; Tsuboi, Seijaku; Hirose, Sho; Soga, Koichi. Department of Psychiatry, Niigata University, Japan **Comparative study of clocapramine and perphenazine on chronic schizophrenia by a double-blind method.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(8):867-874, 1974.

The effect of clocapramine (CCP) and perphenazine (PPZ) on chronic schizophrenia was studied, based on a double-blind experiment in which 66 chronic schizophrenic patients with main symptoms of autism and hypoactivity were treated with levomepromazine for a week followed by CCP or PPZ for 6 weeks. After 6 weeks, 47% of the CCP treated patients improved, as compared to 14% of those who had taken PPZ. CCP also showed significantly better effect on volition and behavior in the patients than PPZ. Both drugs induced an almost equal rate of Parkinsonism (12.5%-17.5%). Among five patients who dropped out, four had been treated with PPZ and had experienced an aggravation of the symptoms or side-effects, and one who was treated with CCP missed taking the drug in the middle of the experiment. 19 references.

223165 WHITE, A. C.; Sims, A. C. P. All Saints Hospital, Birmingham, Enlgand **The use of an orgal long-acting antipsychotic agent, penfluridol, in schizophrenia.** Current Medical Research Opinion. 2:23, 1974.

Results of the once weekly administration of penfluridol, a depot neuroleptic, in 10 cases of chronic schizophrenia are reported. Penfluridol is the first orally administered depot neuroleptic with a 1 week duration of effect. The patients were treated with 20mg - 60mg of the drug once weekly over a 2 month period, and their improvement was assessed via the "Nurse's Observation Scale for Inpatient Evaluation". Eight patients showed significant clinical improvement, even in those cases resistant to previous medication. Penfluridol is of particular advantage in therapy due to its long course of activity. (Journal abstract modified)

223202 Komuku, Tsutomu; Nakao, Takehisa; Kishimoto, Ro; Koga, Itsuyuki; Inagaki, Taku; Motoike, Mitsuo. Department of Neuropsychiatry, Tottori University School of Medicine, Yonago, Japan **Treatment results of L-dopa on schizophrenia.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(10):1115-1124, 1974.

The simultaneous administration of L-dopa and strong tranquilizers to 94 schizophrenic adults who failed to respond to any medication resulted in 21 positive effects, 69 with no significant improvement, and four adverse effects. Side-effects were seen in 17% of the Ss. Improvements were shown primarily in the areas of rapport with others, conduct and behavior. Although only about 25% of the patients responded positively to treatment, it is concluded that the use of L-dopa with other medication was successful since these patients had previously failed to respond to treatment. 16 references. (Author abstract modified)

224085 Bazhin, E. F.; Gorskiy, G. D. Leningradskogo nauchno-issledovatel'skogo psikhonevrologicheskogo instituta im. V. M. Bekhtereva, Leningrad **/Atropine coma treatment of schizophrenic patients with a sluggish development and obsessive syndromes./** Lecheniye atropinovymi komami bol'nykh vyalotekushchey shizofreniyey s navyazchivostyami. Zhurnal nevropatologii i psikhiatrii imeni S. S. Korsakova (Moskva). 75(5):745-747, 1975.

The effectiveness of atropine comatose therapy was investigated in 20 schizophrenic patients with sluggish development and obsessional symptoms. All subjects had previously proved unresponsive to both insulin and neuroleptic treatment. Following comatose therapy, a complete disappearance of obsession was manifested in six patients; a significant alleviation of obsession intensity was noted in six other patients. High doses of atropine were tentatively concluded to be effective in curbing obsessional - phobic symptomatology through the antihallucinogenic properties of the drug. 17 references. (Journal abstract modified)

224383 Askarov, A. A. Kafedra psikhatrii Tashkentskogo instituta usovershenstovaniya vrachey, Tashkent **/Treating patients with a sluggish form of schizophrenia./** O lechenii bol'nykh vyalotekushchey shizofreniyey. Meditsinskiy Zhurnal Uzbekistana (Tashkent). No. 5:13-15, 1975.

The effectiveness of various therapeutic methods was investigated in treating patients with sluggish forms of schizophrenia. All participants were exposed to clinical - catamnetic observation. Treatment was administered according to an evaluation of the patient's psychopathological condition. Physiotherapy was found to be most effective in treating patients in the early stages of the disease. Schizophrenics with neurotic like symptoms were found responsive to psychopharmacological therapy. Patients with more acute symptoms were responsive to antidepressants.

224417 Watt, David C. no address **Time to evaluate long-acting neuroleptics?** Psychological Medicine (London). 5(3):222-226, 1975.

The widespread use of long-acting neuroleptics for schizophrenic patients in North America and Europe is discussed. Severe reactions have been noted in some subjects on neuroleptics from whom antiparkinsonian medication was withdrawn. The impact on families and relatives of schizophrenics who have been released on drugs is considered. It is concluded that long-acting neuroleptics may become too uncritically accepted as the standard treatment for schizophrenia. It is recommended that pharmacological and clinical measures to brought to bear on the problem of their evaluation. The incidence of dyskinesia, long-term maintenance problems, and necessary duration of supervisory treatment with long-acting neuroleptics are also considered. 74 references.

224548 Tokizawa, Tetsuya. Ibaragi Tomobe Hospital, Tomobe-cho, Nishiibaragigun, Ibaragi, Japan **Treatment experience of chronic schizophrenia with penfluridol.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(9):997-1007, 1974.

An experiment is reported in which 13 patients with schizophrenic histories of 10 to 20 years and main symptoms of dull emotion, autism and hypoactivity were treated with penfluridol once or twice a week for 3 to 37 weeks. Penfluridol was effective with catatonic and paranoid types of schizophrenia and not effective with hebephrenic types of schizophrenia This drug was most effective in doses of 20mg a week, stimulated emotion and volition and improved behavioral aspects. Aggravation consisted of revival of abnormal experiences due to increase of mental excitation. Side-effects were minor and did not require termination of treatment. 7 references.

224549 Yoshida, Toshihiko; Tanaka, Kunio; Itonaga, Yoshiaki; Ikuzawa, Masao. Fukuoka Prefectural Dazaifu Hospital, Dazaifu-cho, Tsukushigun, Fukuoka, Japan **Comparison of the remedial results of clofluperol and haloperidol for schizophrenia by double-blind test method.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(9):987-996, 1974.

A double-blind experiment is reported in which 137 schizophrenic patients were treated with haloperidol (HL) or clofluperol (CL) for 8 weeks. HL was more effective on emotional and communicational aspects than CL, but no significant difference in overall effects between the two drugs was observed. Both drugs induced sleep disturbance, parkinsonism, and akathisia in about half of the patients, but HL induced more cases of vomiting than CL. 11 references.

224831 Sakalis, George; Chan, T. L.; Sathananthan, Gregory; Schooler, Nina; Goldberg, Solomon; Gershon, Samuel. Department of Psychiatry, New York University Medical Center, New York, NY **Relationships among clinical response, EPS, and plasma CPZ and CPZ metabolite ratios.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 165).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, a paper was presented reporting an attempt to investigate any possible relationship among extrapyramidal syndrome, subclinical hypokinesia, clinical response, and metabolite plasma level ratios in schizophrenic patients treated with chlorpromazine. Active and inactive metabolites, as well as unconjugated glucuronides were included. It was concluded that this approach seems more promising than correlating individual metabolites due to the wide interpatient variation in plasma levels. (Journal abstract modified)

224908 Burgoyne, Rodney W. Department of Psychiatry, University of California, Los Angeles, CA **Effect of drug ritual changes on schizophrenics.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (254-255).

At the 128th Annual Meeting of the American Psychiatric Assocation, Anaheim, California, May 1975, a paper was presented reporting the effect of changing the medication ritual of stabilized chronic schizophrenic patients treated in an outpatient clinic. Focus was on the effect of the nonspecific factors incident to the administration of maintenance drugs by correlating medication ritual changes to attendance patterns. Trends occurred which suggest a change in a long established medication regime might correlate with attendance patterns in some patients, but these were not significant for the group as a whole. No evidence that medication regime manipulation has, on the average, any significant effect on the proximate attendance patterns of these patients was obtained. Statistical analysis of other variables revealed no significant attendance correlation with gender, supporting family, or dosage level of antipsychotic medication. Minority race Ss showed changed attendance patterns significantly more often than Caucasians. Younger patients showed a strong trend towards changed patterns, but this was not significant. (Journal abstract modified)

224955 Simeon, Jovan; Wadud, Abdul; Itil, Turan. Department of Psychiatry, Missouri Institute of Psychiatry, University of Missouri, 5400 Arsenal St., St. Louis, MO 63139 **A comparison of phenothiazines in managing aggressive episodes in schizophrenic patients.** Hospital & Community Psychiatry. 26(9):574, 1975.

Piperacetazine hydrochloride was compared with chlorpromazine by double-blind study in the emergency treatment of aggressive, agitated, and hyperkinetic hospitalized

schizophrenics. Regimens of piperacetazine injectable (2mg/ml) or chlorpromazine (25mg/ml) were applied over a 24 hr period. Treatment and observations were terminated either when the patient became manageable or when the investigator decided that the therapy was ineffective. Several rating scales were completed on each patient before and after the study. Data on the effects of each drug on specific symptoms were subjected to analysis of variance, t-test, and the Wilcoxon matched pairs signed rank test. No statistically significant global improvement occurred with either drug. No significant differences in the efficacy of the two drugs were found. However, patients given piperacetazine showed a trend toward less conceptual disorganization, while those given chlorpromazine tended to show less grandiosity, hostility, and excitement. 3 references.

225325 Ayd, Frank J. Jr. 912 West Lake Ave., Baltimore, MD 21210 **The depot fluphenazines: a reappraisal after 10 years' clinical experience.** American Journal of Psychiatry. 132(5):491-500, 1975.

A review is given of the information gathered during 10 years of clinical experience with depot fluphenazines for schizophrenia. Described are types of patients most likely to benefit from therapy with injectable drugs, the techniques of this therapy, the therapeutic efficacy and side-effects of the drugs, and how they interact with other medication. Depot fluphenazines are considered safe and effective, but caution should be used in determining starting dose and intervals between injections for each patient. Such factors as age, physical condition, diagnosis and drug history must be considered. 51 references. (Journal abstract modified)

09 DRUG TRIALS IN AFFECTIVE DISORDERS

213628 Schildkraut, Joseph J. Harvard Medical School, Boston, MA **Psychopharmacology of biogenic amines in depressions.** Psychopharmacology Bulletin. 11(2):58-59, 1975.

A psychopharmacological attempt to evaluate and develop the catecholamine hypothesis of affective disorders is presented. The hypothesis holds that norepinephrine in the brain plays an important role in the pathophysiology of at least some types of depressive disorders. Results of clinical studies indicate that 3-methoxy-4-hydroxyphenylglycol (MHPG) excretion may provide an index of central noradrenergic activity, particularly in manic-depressives.

213784 Munro, Ronald J. K. Aberdeen Royal Infirmary, Aberdeen, Scotland **Acute hypomania.** Nursing Times (London). 71(1):14-16, 1975.

The case history of a man suffering from acute hypomania is presented. The subject was detained in a psychiatric hospital after having been arrested for causing a breach of the peace. The symptoms of the disorder are outlined, and the manifestation of overactivity and sudden mood changes is stressed. Chemotherapy and electroconvulsive treatment were used in this case, including chlorpromazine and haloperidol, and orphenadrine to control possible side-effects. After a dramatic reaction to electroconvulsive therapy, chemotherapy was discontinued, except for a dose of lithium carbonate once a day. Some improvement in the subject's condition was observed and it is expected that he will be released in the care of his brother. 2 references.

213918 Sachar, Edward J.; Altman, Norman; Gruen, Peter H.; Glassman, Alexander; Halpern, Frieda S.; Sassin, Jon. Bronx Municipal Hospital Center, Pelham Parkway E and Eastchester Road, Bronx, NY 10461 **Human growth hormone response to levodopa: relation to menopause, depression, and plasma dopa concentration.** Archives of General Psychiatry. 32(4):502-503, 1975.

Human growth hormone (HGH) response to levodopa (with consideration of plasma dopa concentration) was studied in postmenopausal women and age matched men in three categories: unipolar depressed, bipolar depressed, and normal. After ingestion of 500mg of levodopa, postmenopausal women had significantly diminished HGH responses as compared with those of the age matched men; the differences between the groups were not related to plasma dopa concentrations. The HGH responses to levodopa of age matched unipolar and bipolar depressed men, and of unipolar depressed postmenopausal women, did not differ significantly from their respective normal control groups. Depressive illness of these types does not appear to affect the HGH response to levodopa, once the effect of the menopause is taken into account. 13 references. (Author abstract modified)

214009 Dittrich, A.; Bickel, P.; Zimmer, Dagmar. Psychiatrische Universitatsklinik, Forschungsdirektion, Postfach 68, CH-8029, Zurich **/Effects of (-)delta9-trans-tetrahydrocannabinol (delta9-THC) on tests of psychoticism: a study of Eysenck's drug postulate on the effects of hallucinogens in relation to psychoticism./** Effekte von (-)delta9-Tetrahydrocannabinol (delta9-THC) auf psychotizismus-Tests: eine Untersuchung des Eysenckschen Drogenpostulats uber Beziehungen zwischen Halluzinogenwirkung und Psychotizismus. Psychopharmacologia (Berlin). 40(4):351-358, 1975.

In a double-blind study on 36 volunteers the effects of (-)delta9-trans-tetrahydrocannabinol (THC) on objective and performance tests measuring psychoticism according to Eysenck were assessed. The hypothesis was tested that subjects treated with THC differ from normals. Confirmation was obtained in only 5 out of 19 variables. Four of these five variables may be considered as tests of concentration. (Author abstract)

215065 Misurec, J.; Nahunek, K.; Kamenicka, V.; Chmelar, M. Psychiatric Clinic Brno-Bohunice, Jihlavska 102, Czechoslovakia **Influence of Azaphen, a new antidepressive drug, on the human EEG.** Activitas Nervosa Superior (Praha). 16(4):245-246, 1974.

At the 16th Annual Psychopharmacological Meeting Jesenik, 1974, a paper was presented which reported the effects of Azaphen on the human electroencephalogram (EEG) in 19 hospitalized patients, aged 20 to 75, suffering from involutional melancholia and endogenous depression. It was concluded that low doses of Azaphen have an activating effect, and that increase of slow activity in the EEG when higher doses were given may be related to its sedative properties. The activating properties in low dose therapy make Azaphen a drug of choice in mild depressions, coupled with a lowered vigility as seen in many mild organic psychosyndromes, especially in involution or some neurasthenic syndromes.

215148 Jepson, K. Sheffield, England A **comparative study of clomipramine (Anafranil) capsules and tablets.** Journal of International Medical Research (Cambridge). 3(Suppl.1):27-35, 1975.

A comparative study of clomipramine (Anafranil) capsules and tablets is reported. Two hundred and seven patients were admitted to a multicenter clinical trial, lasting four weeks, in which tablet and capsule formulations of clomipramine were compared. Findings indicate that both were equally effective

in relieving depression. For all patients irrespective of formulation there was a 27% improvement in symptom scores after 1 week, 52% after 2 weeks, and 68% after 4 weeks. Fifty eight patients were lost to the trial, 40 because of side-effects. A small population of nonresponding patients was identified for whom clomipramine therapy produced no amelioration of symptoms but simply intolerable side-effects. 7 references. (Author abstract modified)

215149 McMillin, W. P. Belfast, Northern Ireland **A comparison of a divided and a single-dose regime of clomipramine (Anafranil).** Journal of International Medical Research (Cambridge). 3(Suppl.1):36-46, 1975.

In order to compare a single daily dose of 75mg of clomipramine (Anafranil) with a divided dose regime, 103 patients were admitted to a multicenter clinical trial, of one month's duration, conducted in general practice. Findings indicate no difference in the efficacy of the two regimes in relieving depression. It is noted that 23 dropouts were due to side-effects, and that there was a problem of initial tolerance in the single dose group. It is recommended that the full dose be reached incrementally. (Author abstract modified)

215150 Gringras, M. Poynton, Cheshire, England **A comparison of a low and high dosage regime of clomipramine (Anafranil).** 3(Suppl.1):47-54, 1975. Journal of International Medical Research (Cambridge).

One hundred and twenty two patients were admitted to an open comparative study of a low dosage (10mg three times daily) and a high dosage (25mg three times daily) regime of clomipramine (Anafranil). Findings indicate that both were equally effective in relieving the symptoms of depression. The low dosage was better tolerated initially and led to less drug induced patient withdrawals. 1 reference. (Author abstract)

215455 Saletu, B.; Saletu, M.; Simeon, J.; Marasa, J. Missouri Institute of Psychiatry, University of Missouri School of Medicine, St. Louis, MO **Fluphenazine treatment in the psychotic child: clinical-evoked potential correlations.** Comprehensive Psychiatry. 16(3):265-278, 1975.

The mode of action of fluphenazine on the clinical symptomatology and brain activity of the psychotic child was studied, with special interest in the relationship between clinical changes and alterations in the visual evoked potential (VEP) during treatment. Ten hospitalized psychotic boys with an age range of 6 to 15 years were studied. Results demonstrate that fluphenazine is of significant overall therapeutic benefit and improves detailed clinical symptomatology of psychotic children as rated independently by the psychiatrist, nurse, parent, and teacher. The overall clinical symptomatology improved as early as the first week and was even more improved in the fourth week. Comparison between VEP measurements of psychotic children on placebo and on fluphenazine with age matched and sex matched normal children suggests that the fluphenazine induced latency and amplitude increases represent a shift of the children's brain function toward the normal side. 52 references.

215699 Lehmann, Heinz E.; Ban, Thomas A.; Schwartz, George V. Division of Psychopharmacology, Department of Psychiatry, McGill University, Montreal, Quebec, Canada **Psychotherapeutic profile of a new psychoactive drug trazodone (AF-1161).** International Pharmacopsychiatry (Basel). 10(1):42-53, 1975.

In a systematic clinical study, including four uncontrolled clinical trials with psychiatric patients belonging to four different diagnostic groups, trazodone, the first triazolopyridine compound subjected to clinical investigation, was found to be a therapeutically effective psychoactive drug. Since the most consistent therapeutic action of trazodone was seen to be in the depressive syndrome, i.e.,guilt feelings, motor retardation and depressive mood, it was suggested that trazodone has a therapeutic effect on depressive symptoms whether they occur in depression, neurosis, organic brain syndrome or schizophrenia. (Author abstract)

215700 Rees, J. A.; Marsh, B. D. Research Department, The Boots Company Ltd., Nottingham, England **The outcome of dothiepin treatment in 1,900 depressed patients.** International Pharmacopsychiatry (Basel). 10(1):54-57, 1975.

One thousand, nine hundred and sixty five depressed patients took part in a multicenter study of dothiepin hydrochloride, which involved 392 doctors. The results indicated that a large percentage of patients improved as measured by all the assessments and no serious or adverse effects were encountered. A good correlation was seen between the global scale and the Rockliff depression scale; and also between the final mean Rockliff score and the number of patients stopping therapy due to recovery, and continuing treatment until recovery, at the final assessment. 1 reference. (Author abstract)

216373 Bunney, William E., Jr.; Kopanda, Richard T.; Murphy, Dennis L. Adult Psychiatry Branch, DCBR, National Institute of Mental Health, Bethesda, MD 20014 **Sleep and behavioral changes reflecting central receptor hypersensitivity following catecholamine synthesis inhibition in man. (Unpublished paper).** Rockville, MD, NIMH, 1975. 13 p.

Sleep was measured in depressed and manic patients following discontinuation of alpha-methyl-para-tyrosine (AMPT), a specific inhibitor of the synthesis of the neurotransmitters norepinephrine and dopamine. A marked decrease in total hours of sleep was found on days three and four following discontinuation of AMPT, but discontinuation of two precursors of biogenic amines, L-DOPA and L-tryptophan produced no changes in total sleep. It is suggested that the decrease in sleep following AMPT may result from catecholamine neuronal receptor hypersensitivity induced during AMPT treatment. Animal data consistent with this hypothesis are reviewed. The importance of studying rebound phenomena following psychoactive drug application, and practical therapeutic implications of these findings are discussed. 49 references. (Author abstract modified)

216463 Pearce, J. B.; Linford Rees, W. no address **A double-blind comparison of three times daily and single night dosage of the tricyclic antidepressant dothiepin.** Journal of International Medical Research (North Hampton). 2:12-19, 1974.

The advantages of administering a single daily dose of dothiepin as opposed to the same dose administered three times daily were investigated, and dothiepin was compared with a placebo. The 62 Ss were tested daily for 5 weeks. The most favorable results were observed in patients taking a single dose in the evening. This single administration was well tolerated and was effective in improving the depressive symptoms. The advantages of this type of administration are discussed.

216747 Rybakowski, Janusz; Sowinski, Jerzy; Makowska, Krystyna. Dept. of Psychiatry, Medical Academy, Poznan, Po-

land **Free thyroxine index and absolute free thyroxine in patients with affective disorders treated with lithium carbonate.** Materia Medica Polona (Warszawa). 6(4):271-275, 1974.

Thyroxine indices including total thyroxine, free thyroxine index and absolute free thyroxine were investigated in 24 patients with affective disorders before and following 14 days of lithium carbonate treatment. Mean prelithium values in the total population were significantly lower than normal, being the lowest in manic, slightly greater in bipolar depressive, and low borderline normal in unipolar depressive patients. After 14 days of lithium therapy there was a small reduction of mean values in the total population. In individual patients, there was a tendency for lowest lithium values to increase, while others decreased after lithium. High occurrence of low thyroxine indices in affective patients is stressed. It is suggested that thyroid pathology may be of pathogenetic importance in some patients. 26 references. (Author abstract)

216758 Zarifian, E.; Cottereau, M. J.; Loo, H.; Ginestet, D.; Deniker, P. Service hospitalo-universitaire de Sante mentale et de Therapeutique, Hopital Sainte-Anne, 75674 Paris Cedex 14, France /**An attempt to verify the antidepressant action of the hypothalamic thyrostimulin (thyrotropin releasing factor or TRF) in melancholic states.**/ Essai de verification de l'action thymoanaleptique de la thyrostimuline hypothalamique (thyrotropine releasing factor ou TRF) dans les etats melancoliques. Encephale (Paris). 1(1):9-14, 1975.

At the Ninth Congress of the International College of Neuro-psychopharmacology, Paris, July 1974, a paper was presented in which the question of whether the thyrotropin releasing factor (TRF) has a real antidepressant effect and if repeated administration could cure a depressive state was discussed. TRF was used either intravenously in a dose of 1mg/day or orally in a dose of 30mg/day with 18 monopolar or bipolar melancholic patients. Treatment lasted from 8-21 days. Four favorable results were obtained between the 2nd and 6th days, all with bipolar melancholics. In the other cases, the results, although very limited, open perspectives concerning a physiological substance whose site and modalities of action are fairly precisely known. (Author abstract modified)

216760 Maurel, H.; Pujol, B. 09190 Saint-Lizier, France /**An attempt to classify sultopride among current neuroleptics.**/ Essai de situation du sultopride parmi les neuroleptiques actuels. Encephale (Paris). 1(1):19-24, 1975.

At the Ninth Congress of the International College of Neuro-psychopharmacology, Paris, July 1974, a paper was presented in which preliminary clinical investigations of sultopride, a new substituted benzamid related to sulpiride, were reported. The drug was administered to 39 hospitalized psychotic patients. The drug's antipsychotic action seems more regular and qualitatively very different from that of sulpiride. Sultopride acts as a powerful neuroleptic, having both sedative and "incisive" properties. Its effectiveness in treating states of excitation, notably in acute mania, is particularly interesting. Its side-effects are frequent and varied: somnolence, extrapyramidal effects requiring the use of antiparkinsonians, and psychic side-effects, consisting of depressive and anxious modifications of mood. The drug controlled excitation in 11 manic and hypomanic syndromes between the first and third day with oral doses of 1200-1800mg. Thymic inversion was observed in 8 cases of bipolar affective disorder.

216761 Lambert, P.-A.; Carraz, G.; Borselli, S.; Bouchardy, M. Hopital de Bassens, Clinique de Bressieux, Chambery-Savoie, France /**Dipropylacetamide in treating manic-depressive psychosis.**/ Le dipropylacetamide dans le traitement de la psychose maniaco-depressive. Encephale (Paris). 1(1):25-31, 1975.

At the Ninth Congress of the International College of Neuro-psychopharmacology, Paris, July 1974, a paper was presented in which the use of dipropylacetamide, first used in treating epilepsy, was discussed as being a normalizing agent in the periodic evolution of manic-depressive psychosis. The drug's therapeutic action has several effects: 1) total suppression of attacks; 2) reduced intensity of these attacks; 3) increasing the interval between attacks; 4) greater response to antidepressants and neuroleptics which can be prescribed in much smaller doses. Manic forms respond more than depressive forms to the drug. The average doses are around 900mg. Precautions are necessary when beginning treatment due to the use of sedatives, but treatment is subsequently very well tolerated and accepted by patients for periods of several years without the need for biological controls. Combining lithium with dipropylacetamide often yields remarkable results. 29 references. (Journal abstract modified)

216769 Burton, P. Sanitas, Clinique neuro-psychiatrique, Dave, Belgium /**Clinical experimentation with a sustained release lithium carbonate.**/ Experimentation clinique d'un carbonate de lithium retard. Revue Medicale de Liege (Liege). 30(3):79-80, 1975.

The use of sustained release lithium carbonate (LC) in treating depression was investigated in 21 patients. Mood stabilization was noted in all patients, with a decrease in manic or depressive attacks. Side-effects were minimal with doses of two or three 400mg tablets per day. Six patients were treated with nonsustained release LC. With this type of LC, it was difficult to establish the correct dosage, and side-effects were more frequent with poor gastric tolerance and digital tremor. These 6 cases did not show the same psychological stability that the 21 cases treated with sustained release LC did. The difficulty of maintaining a proper lithium level with ordinary LC makes the use of sustained release LC preferable since it ensures serum lithium levels which are almost constant and minimal side-effects. 15 references.

217114 Okuma, Teruo; Takeshita, Hisayoshi; Nakao, Takehisa; Uchida, Yasunori; Kishimoto, Akira; Fukuhara, tomokazu; Matsushima, Yoshihiko. Department of Neuropsychiatry, Tottori University School of Medicine, Japan **The effect of lithium carbonate on the electroencephalogram of manic-depressive psychotics.** Clinical Psychiatry (Tokyo). 16(4):397-408, 1974.

The effect of lithium carbonate (LC) on the EEG of 44 manic-depressive patients was studied, based on the EEG recordings of the patients before, during and/or after treatment with LC for 3 days to 2 years and 3 months, and with or without combined psychotropic drugs. Among 19 patients whose EEG was recorded only during LC treatment, 88% showed changes in alpha wave. Among 23 patients whose EEG was recorded before and during LC treatment, 47.8% showed normal EEG before LC treatment and abnormal EEG after LC treatment. Most of the patients who showed abnormal EEG were young, and two patients who showed general epileptic seizure discharge were under 20 years of age. All the patients who showed abnormal EEG eventually resumed normal EEG after termination of LC treatment. No significant relation between onset of EEG abnormality and clinical condition, dose of LC, side-effect from LC or clinical effect of LC was observed. 32 references.

217171 Lambert, P. A.; Cabrol, G.; Mallion, Y.; de Maximy, B. no address **/Clinical study of pimozide./** Etude clinique du pimozide. Information Psychiatrique (Lyon). 50(6):651-654, 1974.

Pimozide, a new neuroleptic drug, was clinically studied in 67 Ss with affective disorders. Excellent results were obtained in 18 cases, and good results in 23 cases. The drug was most effective in treating chronic delirium, with an effectiveness of 80%. The drug is very useful in treating outpatients, due to its rapid action. It is particularly effective in evolving schizophrenic processes with easily reversible symptomatology, and is also indicated for behavioral disturbances, particularly in epilepsy. Side-effects of the drug were negligent and easily corrected. 12 references.

217354 Watanabe, Shosuke; Nabeyama, Toshiro; Chuta, Masaki; Nakajima, Yoko; Hoaki, Takayuki. Department of Neuropsychiatry, Okayama University School of Medicine, Japan **Relationship between serum lithium level and clinical response on depression treated with lithium carbonate.** Clinical Psychiatry (Tokyo). 16(10):887-892, 1974.

The relationship between serum lithium level and clinical state of depression was studied. Ss were 25 mildly depressive individuals orally treated with lithium carbonate (450-900mg/day) for 5 weeks. Serum lithium level prior to treatment was unrelated to depressive state. No significant differences were observed between therapeutic and ineffective serum lithium levels. The occurrence of side-effects also appeared unrelated to serum lithium level. 19 references.

217450 Angst, J.; Dittmer, Th. L. J.; Heinrich, K.; Hippius, H.; Siebel, I.; Woggon, B. Psychiatrische Klinik, Universitat Zurich, 8000 Zurich, Switzerland **/Clinical trial of lofepramin versus imipramine./** Klinische Prufung von Lofepramin im Vergleich zu Imipramin. International Pharmacopsychiatry (Basel). 10(2):65-71, 1975.

The effects and side-effects of lofepramin were compared to those of imipramine in a double-blind trial. Forty nine hospitalized patients, suffering from endogenous depression, were treated for 20 days with 210mg lofepramin daily and 52 other patients with 150mg imipramine daily. The results of the repeated psychiatric examinations were documented using the adenosine monophosphate system. Both substances proved to have high antidepressant effects and showed no significant difference in the quality of their effects. 5 references. (Journal abstract)

217477 Olivier-Martin, R.; Marzin, D.; Buschsenschutz, E.; Pichot, P.; Boissier, J. Clinique des Maladies mentales et de l'Encephale, 100, Rue de la Sante, F-75 Paris 14e, France **/Plasma levels of imipramine and desmethylimipramine and antidepressant effect during controlled therapy./** Concentrations plasmatiques de l'imipramine et de la desmethylimipramine et effet anti-depresseur au cours d'un traitement controle. Psychopharmacologia (Berlin). 41(2):187-195, 1975.

Plasma levels of imipramine and desmethylimipramine (DMI) and antidepressant effect during controlled therapy were examined. Depressed inpatients (N=24) received a standardized treatment by imipramine, six among them receiving also levomepromazine. Plasma concentrations of imipramine and DMI were controlled weekly during the study, and standardized assessments of clinical state were made by a psychiatrist who was unaware of biochemical findings. Interaction between the antidepressant and neuroleptic metabolism is shown by a significant increase of DMI levels, though the clinical effect of the drug association could not be asserted. The therapeutic effect seems mainly dependent upon the etiology of the depression. Endogeneous depressions improve more than other types. Among endogenous depressions a significant correlation was found between the degree of clinical improvement after 3 weeks and DMI level, sum of imipramine plus DMI level, but not with concentration of imipramine alone. 14 references. (Author abstract)

218041 Paykel, E. S.; DiMascio, A.; Haskell D.; Prusoff, B. A. Dept. of Psychiatry, St. George's Hospital, London SW17 0QT **Effects of maintenance amitriptyline and psychotherapy on symptoms of depression.** Psychological Medicine (London). 5(1):67-77, 1975.

Findings from a study of maintenance amitriptyline and psychotherapy on symptoms of depression are presented. Depressives responding to initial treatment were maintained on amitriptyline for 8 months, withdrawn double-blind to placebo after 2 months or withdrawn overtly onto no medication. In each group half of the Ss received weekly psychotherapy and half were seen once monthly. Effects on symptom ratings were examined. Maintenance amitriptyline gave a significant advantage over early withdrawal in preventing symptom recrudescence. There were no differences between double-blind or overt withdrawal. There were no interactions between drug withdrawal and psychotherapy. Psychotherapy produced no significant advantages over low contact on symptoms although it did improve social adjustment ratings reported elsewhere. 24 references. (Author abstract modified)

218120 Vogel, Gerald W.; Thurmond, Arthur; Gibbons, Pauline; Sloan, Katherine; Boyd, Mary; Walker, Margaret. Sleep Lab, Georgia Mental Health Institute, 1256 Briarcliff Road NE, Atlanta, GA 30306 **REM sleep reduction effects on depression syndromes.** Archives of General Psychiatry. 32(6):765-777, 1975.

Thirty four endogenous and 18 active, depressed patients (hospitalized and nonschizophrenic) were treated in a double-blind, crossover study of the hypothesis that rapid eye movement (REM) sleep reduction (by awakenings) relieves depression. In the endogenous group, but not in the reactive group, subjects deprived of REM sleep for 3 weeks improved significantly more than control subjects awakened from non-REM sleep. Therapeutic efficacy of REM sleep reduction appeared similar to reported efficacy of imipramine hydrochloride treatment of depression. Eight of nine endogenous patients, unimproved by REM sleep deprivation, did not improve with imipramine. Results suggest that: 1) substantial REM sleep reduction has antidepressant activity; and 2) since imipramine and other antidepressant drugs reduce REM sleep much more so than nonantidepressant drugs, an antidepressant mechanisms of drugs resides in their capacity to substantially reduce REM sleep. 95 references. (Author abstract modified)

218123 Ostow, Mortimer. 5021 Iselin Avenue, Riverdale, NY 10471 **Treating depression with tranquilizers: with dissenting view of lithium carbonate therapy.** New York State Journal of Medicine. 75(5):693-696, 1975.

It is argued that the use of tranquilizers to treat depression is superior to lithium carbonate therapy. The prompt action and negligible side-effects of small doses of thioxanthene or phenothiazine are cited. It is maintained that lithium lacks the special affinity of tranquilizers for manic-depressions and that its action in the treatment of mania is surpassed by moderate to high doses of tranquilizer. It is also noted that, for the deterrence of relapse during remission, low doses of tranquil-

izer are less toxic and more flexible, although no less potent than lithium. 4 references. (Journal abstract modified)

218129 Shopsin, Baron; Gershon, Samuel. Department of Psychiatry, New York University Medical Center, 550 First Avenue, New York, NY 10016 **The current status of lithium in psychiatry.** American Journal of the Medical Sciences. 268(6):306-323, 1974.

The current use of lithium in the treatment of the manic phase of manic-depressive psychoses is described. The effectiveness of lithium in acute mania, in endogenous depression, in prophylaxis against recurrent depression and/or mania, and in psychiatric disorders other than mania is discussed. The pharmacology of the lithium ion is mentioned. It is concluded that the special properties of the lithium ion derived from biochemical and pharmacological research provide new insights about the molecular biology of a number of organ systems. 173 references.

218362 Ota, Fujio. Dept. of Neuropsychiatry, Jikei Univ. School of Medicine, Nishishinbashi 3-25-8, Minato-ku Tokyo, 105 Japan **Mood and catecholamine -- nonsimplicity of their relationship.** Journal of Japanese Psychosomatic Society (Fukuoka). 15(1):26-32, 1975.

Differences in urinary catecholamine (CA) level in depressives treated with antidepressants were investigated. Some cases showed clinically complete remission with urinary CA returning to the normal level (19.2%). Some (15.4%) cases showed clinically complete remission without marked change in urinary CA level. In other (42.3%) cases, either the clinical remission or urinary CA level hardly returned to the normal. In some cases (23.1%), there was a marked change in CA level, although remission was clinically difficult. It is concluded that the relation between mood and CA is not simple. Besides CA, physical, psychological, and environmental factors are considered to be involved. It is concluded that CA may determine mood but cannot be regarded as the only determining factor. 18 references. (Journal abstract modified)

218556 Hullin, R. P.; McDonald, R.; Allsopp, M. N. E. Regional Metabolic Research Unit, High Royds Hospital, Menston, Ilkley, LS29 6AQ, England **Further report on prophylactic lithium in recurrent affective disorders.** British Journal of Psychiatry (London). 126:281-284, 1975.

The effectiveness of lithium as a prophylactic agent against recurrent affective disorder was examined. A group of 95 Ss was studied for an average period of 50 months. The number of admissions to and time spent in a psychiatric hospital during lithium treatment was compared in each S with the situation in an equivalent period immediately prior to the commencement of prophylactic treatment. The average number of admissions for episodes of depression and/or mania fell from 4.1to 0.7and the average time spent in hospital from 30 to 4 weeks. Sixty six of the Ss in the group were not readmitted to the hospital while receiving lithium; these total responders included all of the nine unipolar manics and 11 unipolar male depressives. Patients with bipolar manic-depressive psychosis had the lowest percentage of total responders. The occurrence of long-term side-effects of lithium on thyroid function and calcium metabolism is discussed. 7 references. (Author abstract modified)

218682 Davis, Dave M. Peachtree and Parkwood Mental Health Center, 1999 Cliff Valley Way, N.E., Atlanta, GA 30329 **Experience with 20 patients treated with lithium carbonate.** Journal of the Medical Association of Georgia. 64(5):134-136, 1975.

Results of long-term use of lithium with 20 manic-depressive patients are presented. In the manic-depressive group, the only patients who were rehospitalized, were three who discontinued their medication on their own and experienced an immediate resultant manic attack, despite constant repetition by the therapist of the need to continue on the medication. It is concluded that lithium carbonate was successful in improving the functioning of the manic-depressive group. Side-effects are tablated, and since they were minimal larger doses are recommended. 2 references. (Author abstract modified)

218770 Raskin, Allen; Crook, Thomas H. Psychopharmacology Research Branch, 5600 Fishers Lane, Rm 9-101, Dept. of Health, Education, and Welfare, Rockville, MD 20852 **Antidepressants in Black and White inpatients: differential response to a controlled trial of chlorpromazine and imipramine.** Archives of General Psychiatry. 32(5):643-649, 1975.

Differential effects of chlorpromazine, imipramine hydrochloride, and a placebo were examined in 159 Black and 555 White depressed patients in a multihospital collaborative study. In making these comparisons, the effects of age and social class were controlled. The major study findings were the differential effects of the active drugs for the Black men and women. Chlorpromazine was the most efficacious treatment for Black women, whereas imipramine was most efficacious for Black men. These differences occurred on global ratings of improvement as well as on specific symptoms such as depression, anxiety, guilt - worthlessness, sleep disturbances, and social participation. Black patients also evidenced a higher improvement rate at 1 week, irrespective of treatment, than did the White patients. Backgrounds and marital status of the patients and symptoms of psychiatric illness were also investigated. 37 references. (Author abstract modified)

218772 Watanabe, Shosuke; Ishino, Hiroshi; Otsuki, Saburo. Kawasaki Medical College, Kurashiki, Japan **Double-blind comparison of lithium carbonate and imipramine in treatment of depression.** Archives of General Psychiatry. 32(5):659-668, 1975.

The antidepressive effects of lithium carbonate were compared to those of imipramine hydrochloride in 64 Japanese depressed patients under double-blind conditions. No significant differences were noted in the overall therapeutic response, depression scale scores, or clinical effects between the two drug groups. Time lapse change, dosage, concomitant symptoms and side-effects of the two drugs are discussed. Graphs depicting the comparative serum lithium levels, clinical therapeutic responses and Hamilton depression scores under double-blind conditions are included. Results of the laboratory findings are compared to earlier studies. 43 references. (Author abstract modified)

218959 Spatz, H.; Heller, B.; Nachon, M.; Fischer, E. Laboratorio de Psicofarmacologia y Neuropsiquiatria Experimental, Hospital Nacional J. T. Borda, Buenos Aires **Effects of D-phenylalanine on clinical picture and phenethylaminuria in depression.** Biological Psychiatry. 10(2):235-239, 1975.

The administration of D-phenylalanine in 11 cases of depression with low urinary phenethylamine output was studied. It was found that the administration of D-phenylalanine to depressed patients in daily oral doses of 100-200mg produced an improvement of the clinical state associated with an increase in the daily urinary phenethylamine output. 13 references. (Author abstract modified)

219365 Van Putten, Theodore. Veterans Administration Hospital, Brentwood, CA **Why do patients with manic-depressive illness stop their lithium?** Comprehensive Psychiatry. 16(2):179-183, 1975.

Six patients with severe manic-depressive illness who refused prescribed treatment with lithium, despite the fact that the drug was established to be of value for each of them, are discussed. Patients with this illness may stop lithium prophylaxis in order to experience a manic reprieve from such dysphoric effects as disappointment, grief, rage, feelings of abandonment, or envy. The common use of denial and the notable lack of self-awareness in these patients, however, suggests that stoppage of therapy is not consciously motivated; the patient usually attributes his interruption of lithium prophylaxis to forgetting or to the belief that he no longer needs it. Since patients tend to discontinue prescribed treatment with lithium at times of life crises, lithium therapy should occur in the setting of an ongoing therapeutic relationship. 16 references.

219521 Hall, R.; Hunter, P. R.; Price, J. S.; Mountjoy, C. P. Endocrine Unit, Department of Medicine, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP, England **Thyrotrophin-releasing hormone in depression.** Lancet (London). No. 7899:162, 1975.

A controlled trial of the effect of thyrotrophin releasing hormone (TRH) on depression was conducted. Ten clinically and biochemically euthyroid patients suffering from severe primary depressive illness with psychomotor retardation and/or depressive delusions were Ss. They received either antidepressants alone or in conjunction with electroconvulsive therapy (ECT). The random allocation to trial treatment was within pairs; each pair was matched for ECT or non-ECT treatment. There was no difference in the initial scores on the seven point global scale and little difference between treatment groups on the initial Hamilton depression scale scores. Analysis of covariance using the Hamilton scores showed no statistically significant difference in outcome between saline and TRH treated groups. The results therefore fail to confirm an antidepressant action for TRH. 8 references.

219960 Yaryura-Tobias, J. A.; Patito, J. A.; Mizrahi, J.; Roger, R. V.; Cappelletti, S. R. 1691 Northern Boulevard, Manhasset, NY 11030 **The action of pimozide on acute psychosis.** Acta Psychiatrica Belgica (Bruxelles). 74(4):421-429, 1974.

The effect of pimozide on paranoid nucleus, hallucinations, aggressiveness, sleep, libido, and the extrapyramidal system was investigated in a population of 10 acute male psychotics. Pimozide in 2mg tablets and placebo were administered orally in one daily dose. Results indicated an aggravation of the psychosis, aggressiveness, insomnia, and increased verbalization and libido. There was a definite increase in gregarious activity. It is suggested that pimozide has similar properties to those of levodopa or amphetamines. It could be used as an adjuvant agent in chronic psychotics with psychomotor retardation, negativism, withdrawal, lack of drive, or loss of "joie de vivre". It seems to have a good resocializing effect without serious untoward effects or toxicity. 24 references. (Author abstract modified)

219961 Cosyns, P. Grensstraat 3, B-3070 Kortenberg, Belgium **A single daily dose of a sustained release form of amitriptyline in depressive illness.** Acta Psychiatrica Belgica (Bruxelles). 74(4):430-436, 1974.

The clinical and therapeutic effects of a single dose of amitriptyline per day, administered in a sustained release capsule, were compared with the effects of standard amitriptyline, administered three times per day. It was concluded that there was no clinical difference between the two methods of treatment either after 3 or after 6 weeks. The use of sustained release amitriptyline may be regarded as an improvement in the treatment of depressive states since the preparation has to be administered only once a day and in a smaller dosage (50mg) than standard amitriptyline (75mg). 4 references. (Author abstract modified)

220367 Ventsovskiy, E. Psikhiatricheskaya klinika Karlova Universiteta, Pilsen, Czechoslovakia **/The significance of psychopharmacology for psychiatric rehabilitation./** Znacheniye psikhofarmakologii dlya psikhiatricheskoy reabilitatsii. In: Kabanov, M., IV Mezhdunar. Simpoz. po Reabilit. Psikhicheski Bol'nykh. Leningrad, Psikhonevrologicheskiy Institut, 1974. 331 p. (p. 24-25).

In a paper presented at the Fourth International Symposium on Rehabilitation of the Mentally Ill held in Leningrad, October 1974, the use of neuroleptics in various mental disorders to accelerate resocialization was described. Drug therapy in combination with personal, occupational and social rehabilitation therapy can be effective in reintegration. Use of these methods with psychotic patients was described. (Journal abstract modified)

220434 Ende, W.; Poppe, W. no address **/Preventive use of lithium in elderly patients./** Die Lithiumprophylaxe im hoheren Lebensalter. In: Kabanov, M., IV Mezhdunar. Simpoz. po Reabilit. Psikhicheski Bol'nykh. Leningrad, Psikhonevrologicheskiy Institut, 1974. 331 p. (p. 235-238).

In a paper presented at the Fourth International Symposium on Rehabilitation of the Mentally Ill held in Leningrad, October 1974, the use of lithium in preventing manic-depressive illness in elderly patients was considered. Case studies demonstrate the efficacy of this drug. Five patients treated during 1970 - 1971 showed no relapses. Similar results were reported for 45 patients who were administered lithium during 1972 - 1973. Individual observation and measurement of blood lithium content make lithium a practical preventive drug for the majority of elderly manic-depressive patients. (Journal abstract modified)

221045 Beckmann, Helmut; St.-Laurent, Jacques; Goodwin, Frederick K. Section of on Psychiatry, Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **The effect of lithium on urinary MHPG in unipolar and bipolar depressed patients.** Psychopharmacologia (Berlin). 42(3):277-282, 1975.

Twenty four hour urinary excretion of 3-methoxy-4-hydroxyphenylglycol (MHPG), the metabolite thought best to reflect brain norepinephrine metabolism, was studied longitudinally in 10 depressed patients before and during the acute and chronic phases of lithium treatment. Five of the patients were identified as bipolar I (prior history of mania), 3 as bipolar II (history of hypomania) and 2 as unipolar (history of depression). During acute lithium administration (first week) there was no consistent pattern of change in MHPG. Comparing the predrug period with the third and fourth week of treatment, all of the responders showed an increase in MHPG, while the nonresponders showed no change or a decrease. It is concluded that the change in clinical state is the most important variable contributing to MHPG changes in these patients. There was a tendency for the pretreatment MHPG excretion to be low in the patients who went on to show a clear cut an-

tidepressant response to lithium compared to those who were unequivocal nonresponders. The predrug MHPG for the bipolar patients (prior history of mania) was significantly lower than the unipolar patients, a difference which apparently contributes to the lower MHPG in the lithium responders, all of whom were in the bipolar group. 44 references. (Author abstract)

221166 Tsuang, Ming T.; Winokur, George. 500 Newton Rd., Iowa City, IA 52242 **Bipolar primary affective disorder.** Journal of Operational Psychiatry. 6(1):47-53, 1974.

The nature of bipolar psychosis or manic-depressive illness is examined. The clinical appearance and course of the illness is described and criteria for diagnosis suggested, stressing that one must be careful to differentiate the illness from a schizophrenic disorder. Etiology may be considered to be distal and proximal. Intensive treatment is not indicated in either mania or depression. The usual treatment for the manic patient is initial administration of a neuroleptic drug followed by electroconvulsive therapy (ECT) if necessary. The treatment of depressive episodes is mainly ECT or tricyclic antidepressants. Use of lithium is recommended in cases with a firm diagnosis of typical affective disorder, but requires careful monitoring. Finally, some areas of current interest in the diagnosis and treatment of such disorders are briefly reviewed. 36 references.

221209 Ichimaru, Seiichi; Ono, Tsuneyuki; Kameta, Hideaki; Kitajima, Shogo; Kudo, Yoshi; Tanimukai, Hiroshi. Department of Psychiatry, Sumitomo Hospital, Japan **Experience with imipramine-N-oxide (IPNO) in treating depressive states.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(8):875-882, 1974.

The effect of imipramine-N-oxide on depressive states was studied, based on an experiment in which 67 patients with endogenous depression, senile depression, neurotic depression, reactive depression, atypical psychosis, presenile depression and organic depression were treated for 7-506 days. Aggravation of symptoms was observed in 4 patients and side-effects were observed in 22 patients. The drug was primarily effective in patients suffering from endogenous depression, presenile depression, neurotic depression and reactive depression. 9 references.

221306 Lingjaerde, O.; Asker, T.; Bugge, A.; Engstrand, E.; Eide, A.; Grinaker, H.; Herlofsen, H.; Ose, E.; Ofsti, E. University of Tromson, 9010 Asgard, Norway **Noxiptilin (Agedal) -- a new tricyclic antidepressant with a faster onset of action? A double-blind, multicentre comparison with amitriptyline.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 8(1):26-35, 1975.

The results of a double-blind trial are reported in which noxiptilin (Agedal) was compared with amitriptyline in hospitalized patients with primary depressive illness. The total improvement was assessed by direct global assessment or by percentage reduction in total score on Hamilton's rating scale for depression. The two drugs did not differ significantly in their effect on any single symptom, nor in their effect on different types of depression. Both drugs had a better effect in patients with a duration of present illness of less than 3 months than in patients with a duration of illness longer than 3 months. Noxiptilin had a significantly better effect than amitriptyline in patients with insidious onset of present illness, whereas there was a strong tendency for a better effect of amitriptyline in patients with a more acute onset of illness. While side-effects were less frequent with noxiptilin, none of the differences reached significance. Noxiptilin is shown to be an effective antidepressive drug with a fast onset of action. 18 references. (Journal abstract modified)

221310 Mattsson, Bengt; Perris, Carlo. Department of Psychiatry, University of Umea, S-901 85 Umea, Sweden **Average evoked responses (AER) and homovanillic acid (HVA) in cerebrospinal fluid (CSF) in a psychotic patient with Addison's disease.** Archiv fur Psychiatrie und Nervenkrankheiten (Berlin). 219(4):351-355, 1974.

Serial determinations of average evoked responses (AER) and homovanillic acid (HVA) in cerebrospinal fluid (CSF) were made during the psychotic period and recovery phase in a patient with Addison's disease. The patient was treated with cortisone continuously and two series of unilateral electroconvulsive treatments without effect in the early case history, finally neuroleptics (haloperidol) induced complete remission. Clinical recovery was accompanied by a seven fold increase of HVA in CSF, AER amplitudes increased by about 30% and AER latencies diminished by about 7%. 4 references. (Journal abstract)

221348 Heimann, H. Clinique psychiatrique, Hopital de Cery, CH-1008 Prilly, Switzerland **/Antidepressive therapy in general practice./** Antidepressive Therapie in der allgemeinen Praxis. Therapeutische Umschau (Revue Therapeutique) (Bern). 31(11):829-832, 1974.

Diagnostic criteria of the depressive syndrome for use by the general practitioner are presented, and directives are provided for proper antidepressive treatment and for treatment when the patient does not respond to antidepressive medication. Remarks are provided about the prophylactic value of lithium, reserving the use of this drug to specialists only. 12 references. (Journal abstract)

221385 Walinder, Jan; Skott, Annika; Nagy, Adam; Carlsson, Arvid; Roos, Bjorn-Erik. Psychiatric Research Centre, University of Goteborg, St. Jorgen's Hospital, Goteborg, Sweden **Potentiation of antidepressant action of clomipramine by tryptophan.** Lancet (London). No. 7913:984, 1975.

A double-blind trial of the treatment of depression with a combination of clomipramine and tryptophan is reported. The depression rating was significantly lower in the tryptophan group than in the control group (treated only with clomipramine). These observations support the hypothesis that a deficiency of 5-hydroxytryptamine (5-HT) occurs in depression and that accumulation of 5-HT at receptor sites counteracts depression. The finding that addition of tryptophan to clomipramine had a more striking effect on the depression - anxiety score than on the retardation rating supports the hypothesis that 5-HT is specifically involved in the regulation of mood. 11 references.

221559 Lundquist, Gunnar A. R. Sodra Asvagen 18, 180 21 Osterskar, Sweden **/Desipramine as an antidepressant in general practice./** Desipramin som antidepressivum i allmanpraxis. Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(4):249-253, 1974.

The effect of desipramine on exogenous depression was examined in a double-blind study of 40 patients. A daily dose of 75-100mg. for 14 days was found to relieve depressive syndrome in 75% of the cases. 8 references.

221650 Smith, A. J.; Bant, W. P. Department of Pharmacology and Therapeutics, Royal Infirmary, Sheffield, England In-

teractions between post-ganglionic sympathetic blocking drugs and antindepressants. Journal of International Medical Research (Northampton). 3(Suppl. 2):55-60, 1975.

An interim report on interactions between postganglionic sympathetic blocking drugs and antidepressants was presented at the Ludiomil Symposium, Straford-upon-Avon, England, June 1974. Under carefully controlled trial conditions, four depressed inpatients who were receiving sympathetic blocking drugs for their coexisting hypertension received challenge doses of maprotiline. One patient showed drug interaction with significant loss of blood pressure control. The preliminary results of this ongoing study confirm previously published work with maprotiline. It is felt that maprotiline should not be administered to patients receiving postganglionic sympathetic blocking drugs without careful observation to detect alterations in blood pressure control. 3 references. (Author abstract modified)

221651 Lauritsen, Bent. Psychiatric Department, Municipal Hospital, Copenhagen, Denmark **Continental hospital studies with maprotiline (Ludiomil).** Journal of International Medical Research (Northampton). 3(Suppl. 2):61-66, 1975.

At the Ludiomil Symposium, held at Stratford-upon-Avon in June 1974, a paper was presented in which the antidepressant effects of maprotiline (Ludiomil) were compared with those of amitriptyline in 211 depressed patients in a multinational, multicenter trial. The duration of the trial was 4 weeks. No significant differences in antidepressive effect were shown between the two drugs, but maprotiline appeared to be less likely to cause unwanted side-effects than amitriptyline. (Author abstract modified)

221652 Trick, K. L. K. St. Crispin's Hospital, Northampton, England **Double-blind comparison of maprotiline (Ludiomil) with amitriptyline in the treatment of depressive illness.** Journal of International Medical Research (Northampton). 3(Suppl. 2):67-70, 1975.

At the Ludiomil Symposium, Stratford-upon-Avon, England, June 1974, a paper was presented in which a double-blind comparison of maprotiline (Ludiomil) with amitriptyline in treating depressive illness was reported. Thirty patients closely matched for age, sex and duration of illness were treated with either amitriptyline or maprotiline. Within the limits of the small number of patients in the trial, maprotiline produced a significantly quicker improvement during the first two weeks as judged by the scores on the Hamilton Rating Scale. Maprotiline showed better tolerability than amitriptyline overall, especially as far as trial dropout rates were concerned. 4 references. (Author abstract modified)

221653 Mathur, G. N. Department of Psychological Medicine, Billinge Hospital, Lancashire, England **A double-blind comparative clinical trial of maprotiline (Ludiomil) and amitriptyline.** Journal of International Medical Research (Northampton). 3(Suppl. 2):71-74, 1975.

At the Ludiomil Symposium, Stratford-upon-Avon, England, June 1974, a paper was presented in which a double-blind comparative clinical trial of maprotiline and amitriptyline was reported. Significant improvement in the patients' depressed states occurred with both treatments, although Hamilton and Beck rating scales failed to show any statistically significant difference between the two drugs. Global ratings showed maprotiline to be superior to amitriptyline. Both drugs were equally well tolerated. 4 references. (Author abstract modified)

221654 Levine, S. Oldham and District General Hospital, Oldham, Lancashire, England **A controlled comparison of maprotiline (Ludiomil) with imipramine avoiding observer bias.** Journal of International Medical Research (Northampton). 3(Suppl. 2):75-78, 1975.

At the Ludiomil Symposium, Stratford-upon-Avon, England, June 1974, a paper was presented in which a controlled comparison of maprotiline with imipramine was reported. The double-blind trial showed both drugs to be equally effective in the treatment of endogenous depression of moderate severity. Maprotiline appears to be maximally effective in the second week of treatment. The trial was designed to avoid rater bias and an inpatient sample was used to reduce the risk of default. 8 references. (Author abstract modified)

221655 Middleton, R. S. W. Department of Geriatric Medicine, St. James's University Hospital, Leeds, England **A comparison between maprotiline (Ludiomil) and imipramine in the treatment of depressive illness in the elderly.** Journal of International Medical Research (Northampton). 3(Suppl. 2):79-83, 1975.

At the Ludiomil Symposium, Stratford-upon-Avon, England, June 1974, a paper was presented in which maprotiline and imipramine were compared in treating depressive illness in the elderly. Twenty eight elderly female depressed inpatients were admitted to a double-blind trial comparing maprotiline 25mg three times daily with imipramine 25mg three times daily administered for a period of 4 weeks. A target symptom scale, a visual analogue scale and global assessment all showed the two drugs to be equally effective. Tolerability was also similar for the two compounds. 2 references. (Author abstract modified)

221656 Jukes, A. M. CIBA Laboratories, Horsham, Sussex, England **A comparison of maprotiline (Ludiomil) and placebo in the treatment of depression.** Journal of International Medical Research (Northampton). 3(Suppl. 2):84-88, 1975.

At the Ludiomil Symposium, held at Stratford-upon-Avon in June 1974, a paper was presented in which maprotiline and placebo were compared in treating depression. Maprotiline dosage was 50mg three times daily. The trial failed to show any significant difference between the test drug and placebo, mainly because of initially dissimilar treatment groups. The maprotiline patients were in general more chronic in their illnesses and the placebo group was mostly inpatients. The study exemplifies the difficulties in assembling matched groups of psychiatric patients. It is suggested that the only satisfactory way to achieve this is by using large numbers with considerable stratification. 9 references.

221657 Crawford, R.; Donald, A.; Forrest, A.; Hay, J. Royal Edinburgh Hospital, Edinburgh, Scotland **A clinical trial of maprotiline (Ludiomil) in the treatment of depressive patients in general practice and the psychiatric clinic.** Journal of International Medical Research (Northampton). 3(Suppl. 2):89-96, 1975.

At the Ludiomil Symposium, Stratford-upon-Avon, England, June 1974, a paper was presented in which a between patient, double-blind trial comparing maprotililine and imipramine over 28 days in treating depressive patients in general practice and the psychiatric clinic was reported. There were similar side-effects in both treatment groups, but skin rashes were more common with maprotiline. There were no significant differences between treatments, but such differences as were observed favored maprotiline. Differences between the surgery

and clinic populations of depressed patients were noted. It appeared that the patients seen at the surgery were more depressed and much more likely to have had a previous episode of psychiatric illness. 9 references. (Author abstract modified)

221658 Murphy, J. E. Northampton, England **A double-blind general practice trial of maprotiline (Ludiomil) against amitriptyline in the treatment of reactive depression.** Journal of International Medical Research (Northampton). 3(Suppl. 2):97-100, 1975.

At the Ludiomil Symposium, Stratford-upon-Avon, England, June 1974, a paper was presented in which a double-blind trial of maprotiline and amitryptyline in treating reactive depression was reported. Maprotiline was shown to be as effective as amitriptyline with a similar incidence and low level of side-effects. The daily dose of both drugs was 150mg in three divided doses; of the 82 patients initially started on treatment, a total of 59 completed a course lasting 3 weeks. The results obtained indicate that maprotiline is a useful drug in the treatment of depressive reaction and further trials are under way with varying dose regimes. 9 references. (Author abstract modified)

221659 Bartholini, E. Medical Department, CIBA-GEIGY, Basel, Switzerland **Once daily dosage with maprotiline (Ludiomil).** Journal of International Medical Research (Northampton). 3(Suppl. 2):101-108, 1975.

At the Ludiomil Symposium, Stratford-upon-Avon, England, June 1974, a paper was presented in which data from international experience with thrice daily as well as single daily administration of maprotiline were presented. Retrospective comparison of the clinical data using single daily dose regimes with those of three times daily administration, in controlled clinical trials and detailed pharmacokinetic experiments, indicate that both single and three times daily administration are equally effective and well tolerated. It may well be that the choice of a certain schedule depends upon the type of patient and/or the treating physician's personal preference. 4 references. (Author abstract modified)

221660 Liebling, L. I. Highcroft Hospital, Birmingham, England **Once daily dosage study with maprotiline (Ludiomil).** Journal of International Medical Research (Northampton). 3(Suppl. 2):109-113, 1975.

At the Ludiomil Symposium, Stratford-upon-Avon, England, June 1974, a paper was presented in which a double-blind trial with maprotiline and slow release amitriptyline was reported. Depressed psychiatric clinic patients received 75mg maprotiline or 50mg slow release amitriptyline at night for a 4 week period. Assessments were made at the beginning of the study and were repeated after 2 and 4 weeks, using the Hamilton Rating Scale for Depression and the Zung Self-Rating Scale. It is concluded that the two drugs are probably equally effective. The conclusion is tenuous, however, due to the problem of small samples with respect to the difficulty of obtaining matched groups. The most effective way of overcoming differences in group profiles is to stratify the sample for important diagnostic features. 4 references. (Author abstract modified)

221661 Low, N. Cranston. Carlton Hayes Hospital, Narborough, Leicestershire, England **An interim report of a double-blind study comparing a once daily dosage of maprotiline (Ludiomil) with amitriptyline thrice daily.** Journal of International Medical Research (Northampton). 3(Suppl. 2):114-119, 1975.

At the Ludiomil Symposium, held at Stratford-upon-Avon in June 1974, an interim report of a double-blind study comparing a once daily dosage of maprotiline (150mg) and amitriptyline (50mg) three times daily was presented. Assessments were made on day 0, 7, 14, 21 and 28 using the Hamilton Rating Scale for Depression. The patient also scored himself twice daily for the first 30 days by using the 10 cm visual analog scale. The results of the comparison of the two drugs show little difference, and an overall assessment of the twice daily 10 cm lines was not possible with so few patients (N=10). 2 references.

221662 Forrest, W. A. CIBA Laboratories, Horsham, West Sussex, England **A comparison between daily and nightly dose regimen of amitriptyline and maprotiline (Ludiomil) in the treatment of reactive depression in general practice.** Journal of International Medical Research (Northampton). 3(Suppl. 2):120-125, 1975.

At the Ludiomil Symposium, Stratford-upon-Avon, England, June 1974, a paper was presented in which a comparison between daily and nightly dose regimens of amitriptyline and maprotiline in treating reactive depression in general practice was reported. The daily dose regimen of 75mg or nightly dose of 50mg of both trial drugs were equally effective therapeutic agents. On physician assessment at day 21, older patients and those with previous episodes of depressive illness fared significantly less well on amitriptyline than on maprotiline. Maprotiline appeared to exert its action more quickly and was significantly more effective at 14 days than amitriptyline. All four treatment groups tolerated the trial compounds well. Maprotiline 50mg nocte was particularly well tolerated, significantly better than amitripytline nocte. 1 reference. (Author abstract modified)

221667 Loo, H.; Ginestet, D.; Cottereau, M.-J.; Colonna, L.; Deniker, P. Service Hospitalo-Universitaire de Sante Mentale et de Therapeutique, Paris **/Pharmacological - clinical interest in the study of 24 hour lithium rate cycles./** Interet pharmacoclinique de l'etude des cycles lithiemiques de 24 heures. Encephale (Paris). 1(2):97-111, 1975.

At the 9th International Congress of Neuropsychopharmacology, Paris, July 1974, a paper was presented in which 24 hour blood lithium cycles were investigated in patients receiving lithium carbonate or lithium gluconate. The morning lithium level was satisfactory for 48 Ss; for 38, the morning lithium level was below the effective zone; for Ss whose morning lithium rate exceeded 1 mEq1 one became equilibrated during the day, and three did not. The hazards of hyperlithium peaks during the day which are sometimes responsible for transient tremors, nausea, and discrete obnubilations are higher with lithium gluconate. Lithium rates have a smaller difference in levels with respect to morning lithium rate when the drug is administered twice; the difference is minimal with three administrations. Variations in lithium rates during the day are reliable in the same S. Determining the lithium rate cycle is important for more validly judging the quality of balancing lithium salt treatment. 6 references.

221718 Hendler, Nelson. Department of Psychiatry, Phipps Clinic, Johns Hopkins Hospital, 601 North Broadway, Baltimore, MD 21205 **Lithium-responsive hyperaldosteronism in manic patients.** Journal of Nervous and Mental Disease. 161(1):49-54, 1975.

Plasma aldosterone levels of seven untreated manic-depressive patients in the manic phase were compared to five untreated schizoaffective patients in the excited phase and 18

controls. Aldosterone was significantly elevated in the manic patients, and elevated in the schizoaffective patients. After 14 days of lithium carbonate therapy, both psychiatric groups showed a significant reduction in plasma aldosterone and a marked clinical improvement. It is concluded that elevated aldosterone is associated with the manic phase of manic-depressive psychosis. 40 references. (Author abstract)

221820 Petterson, U. no address **/Manic-depressive illness./** Manisk-depressiv sjukdom. Stockholm, 1974.

Research studies with 123 manic-depressive patients treated in a Stockholm hospital in 1961-1970 are described. Methodological and clinical concerns are briefly discussed. The prophylactic effect of lithium in the treatment of manic-depressive patients is emphasized throughout, and psychopharmacological research is detailed.

222604 Worrall, Ernest P.; Moody, J. P.; Naylor, Graham J. Lecturer in Psychiatry, The University, Dundee, DD1 4HN, Scotland **Lithium in nonmanic depressives: antiaggressive effect and red blood cell lithium values.** British Journal of Psychiatry (London). 126:464-468, 1975.

A study adding further weight to evidence that lithium has an antiaggressive effect at normal therapeutic dosage in nonmanic depressives is presented. Lithium was given to eight aggressive, nonmanic depressive female defectives in a double blind placebo controlled study. The group as a whole showed a reduction in aggression scores while on lithium: three patients became less aggressive, one became worse and two were unchanged. Both affective and predatory aggression seemed to be reduced. Two patients had to be withdrawn from the trial at an early stage because of the development of neurotoxicity. Red blood cell/plasma lithium ratios showed a wide interpatinet variation in this group of nonmnaic depressives. The implications of this for hypotheses about the mode of action of lithium and its putative specificity for manic-depressive psychosis are discussed. 17 references. (Author abstract modified)

223318 Birch, N. J. Department of Biochemistry, University of Leeds, 9 Hyde Terrace, Leeds LS2 9LS, England **Lithium and magnesium-dependent processes.** Lancet (London). No. 7921:1384, 1975.

Hypotheses on the pharmacological mechanisms of lithium's action on magnesium dependent and calcium dependent processes are discussed. It is felt that, since lithium is effective in the prophylaxis of recurrent affective disorders, it may be used to discover the metabolic defect, if any, in these disorders. 15 references.

223320 Reilly, Terence M. Department of Psychological Medicine, Middlesex Hospital, London W.1 **Pimozide in monosymptomatic psychosis.** Lancet (London). No. 7921:1385-1386, 1975.

The effect of pimozide in treating refractory monosymptomatic psychosis is reported for one patient. The daily dosage of 4mg administered for 9 weeks relieved delusional hypochondriasis and endogenous depression in a 54-year-old female, who was diagnosed as a chronically anxious individual with a strongly obsessional personality but without previous psychiatric history.

224083 Avrutskiy, G. Ya.; Gromova, V. V.; Zaytsev, S. G. Otdel psikhofarmakologii, Moskovskogo nauchno-issledovatel'skogo instituta psikhiatrii, Ministerstva zdravookhraneniya RSFSR, Moscow **/Treatment of depression with pirazidol./** Lecheniye depressiy pirazidolom. Zhurnal nevropatologii i psikhiatrii imeni S. S. Korsakova (Moskva). 75(5):734-741, 1975.

The effectiveness of pirazidol in treating 140 patients with diagnoses of manic-depression, schizophrenia, chronic depression, and organic depression was investigated. The effects of pirazidol administration were also compared with those of triptizol and noveril. Pirazidol, a major thymoanaleptic, was found to exert a therapeutic effect in deep depressions of an endogenous nature. Unlike other antidepressants, pirazidol was found to have a balancing property, due to its simultaneous sedative and stimulating components of action. Due to its absence of cholinolytic side-effects, pirazidol was concluded to be a safer therapeutic preparation than any of the strong tricyclic antidepressants. 4 references. (Journal abstract modified)

224347 Varkonyi, B. Department of Neurology, Hospital and Central Outpatients' Clinic of the Hungarian State Railways, Budapest **Depressions caused by oral contraceptives and their treatment with Origen.** Therapia Hungarica (Budapest). 22(1):21-25, 1975.

The incidence and types of depressions associated with hormonal contraceptives are surveyed, and hypotheses regarding their etiology are discussed. Cases studied were selected by screening a high number of patients whose symptoms could be partly explained by the administration of the oral contraceptives Infecundin, Bisecurin or Cervicundin. A linear correlation between the total hormone content of the contraceptives used and the incidence of depression was established, and the hypotheses explaining this side-effect on psychic grounds alone are rejected. The simultaneous role of hormone effect and sensitive personality is emphasized. The good results obtained with Origen (N-3,4,5-trimetoxy-benzoyl-heptamethylenimine) in oral contraceptive depression cases are described, and it is suggested that, in women susceptible to depression or with depression history, the depression due to contraceptives may be prevented by the prophylactic use of daily 100 mg Origen doses. 47 references. (Author abstract modified)

224393 Hyugano, Shunso; Yuzuru, Michio. Department of Neuro-psychiatry, Tokyo Medical and Dental University, Tokyo, Japan **Treatment of anxiety by Lorazepam.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(11):1245-1255, 1974.

The effect of lorazepam on anxiety was studied, based on an experiment in which 39 patients with vegetative stigmata, neurosis, anxiety neurosis, phobia, depression, schizophrenia and neurasthenia were treated orally for 2-19 weeks. The drug proved effective in the majority of patients, with improvements usually noted within 7 days of the initial treatment. Side-effects were noted in some patients. 14 references.

224423 Shaw, David M.; MacSweeney, David A.; Hewland, Robyn; Johnson, Anthony L. Welsh National School of Medicine, Whitchurch Hospital, Cardiff, CF4 7XB, Wales **Tricyclic antidepressants and tryptophan in unipolar depression.** Psychological Medicine. 5(3):276-278, 1975.

The amine hypothesis of affective disorders was tested in clinical trials which employed drug protocols designed to selectively enhance either adrenergic or serotonegic activity. Depressed patients were given one of the following combinations in an attempt to find a preferential therapy: clomipramine; clomipramine and tryptophan; desipramine and

clomipramine; and desipramine and tryptophan. In no group was there any evidence of accelerated recovery, indicating that the process of conversion to normal mood may be more complex than suggested by most versions of the amine hypothesis. The data are interpreted as confirming results of a pilot study published previously. 8 references. (Author abstract modified)

224424 Bond, P. A.; Dimitrakoudi, Maria; Howlett, D. R.; Jenner, F. A. St. John's Hospital, Stone, Nr. Aylesbury, Bucks., England **Urinary excretion of the sulphate and glucuronide of 3-methoxy-4-hydroxyphenylethyleneglycol in a manic-depressive patient.** Psychological Medicine (London). 5(3):279-285, 1975.

Sulphate and glucuronide conjugates of 4-OH-3-methoxyphenylethyleneglycol (MOPEG) and 4-OH-3-methoxymandelic acid (VMA) were serially studied in the urine of a 41-year-old female manic-depressive patient before and after a therapeutic response to lithium carbonate. Excretion of both conjugates correlates with changes in mood. Possible reasons why sulphate may be a more useful measure of brain activity are stated. Results are consistent with the catecholamine theory of affective disorders and with previous studies in this same laboratory in England. 23 references. (Author abstract modified)

224486 Kessell, A.; Holt, N. F. Dandenong Psychiatric Centre, Cleeland Street, Dandenong, Victoria, Australia 3175 **A controlled study of a tetracyclic antidepressant -- maprotiline (Ludiomil).** Medical Journal of Australia (Sydney). 1(25):773-776, 1975.

A controlled double-blind comparison of maprotiline (Ludiomil) and imipramine in a group of 71 female outpatients with primary depression is presented. Maprotiline was found to be at least as effective as imipramine and significantly better in depressive neurosis. It also showed a bipolar action, being effective in both agitation and retardation. Maprotiline is a dibenzo bicyclo-octadiene, tetracyclic in structure but pharmacologically related to the tricyclic antidepressants. 6 references. (Author abstract modified)

224588 Watanabe, Shosuke; Ishino, Hiroshi. Department of Neuropsychiatry, Kawasaki Medical College, Japan **Affective disorders and lithium ion.** Clinical Psychiatry (Tokyo). 16(12):1028-1052, 1974.

The literature on the relationship between affective disorders and lithium is reviewed. The relationship of lithium and manic-depressive illness, the preventive effect of lithium on manic-depression, and the effect of lithium on other various emotional disturbances are considered. The mechanism of action of lithium and its side-effects are also described. 196 references.

224749 Davenport, Yolande B.; Ebert, Michael H.; Adland, Marvin L.; Goodwin, Frederick K. Section on Psychiatry, Laboratory of Clinical Science, NIMH, Clinical Center, Bethesda, MD **Lithium prophylaxis: the married couples group.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 66-67).

At the 128th Annual Meeting of the American Psychiatric Association, Anaheim, California, May 1975, a paper was presented which reported the usefulness of couples therapy groups in conjunction with lithium treatment in long-term management of married bipolar manic-depressive patients. Over 4 years, three sequential groups of married bipolar patients and their spouses were treated in this manner. None required rehopitalization for depression or mania, or sustained a marital failure since participation. In a second group followed in individual supportive therapy aimed primarily at regulation of medication, two patients required rehospitalization and five sustained separation or divorce. In the remaining group of 42 married bipolar patients referred back to the community, 17 required rehospitilization, and 10 had marital failure. Patients followed in the couples group had a more benign posthospital course compared to the two control gorups whose followup was comparable to community clinic or private care. (Journal abstract modified)

224766 Weissman, Myrna M.; Kasl, Stanislav V.; Klerman, Gerald L. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06520 **Depressed women one year after maintenance therapy.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 88-89).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, May 1976, a paper was presented which described outcomes for 150 depressed women one year after they completed a controlled treatment trial and entered into an eight month prophylactic trial of amitriptyline and psychotherapy. Findings indicate that over 40% of the Ss sought continued outpatient treatment in the followup, usually psychotropic medication and once to twice monthly outpatient visits. Hospitalization was rare. Findings also show that 10% of the patients remained chronically symptomatic, while 30% were asymptomatic over the year. There was a strong relationship between return of symptoms and receipt of treatment in the followup insofar as the more symptomatic patients during followup received more treatment. However, return of symptoms bore no relationship to the type of controlled maintenance therapy. The effectiveness of these therapies for acute and prophylactic treatment and the lack of a differential effect once the treatment ended emphasized the importance of the early treatment of new episodes. (Journal abstract modified)

224769 Kupfer, David J.; Foster, F. Gordon; Reich, Louis; Weiss, Brian. Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA 15213 **EEF sleep changes as predictors in depression.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 92-93).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, May 1975, a paper was presented in which the usefulness of electroencephalogram (EEG) sleep changes as predictors of depression was described. After 3 weeks of amitriptyline administration, patients were divided into those who responded markedly and those in whom little change could be noted. Comparison of sleep in the premedication phase with the first two nights of drug administration showed that the good response group had a marked decrease in percentage of rapid eye movement (REM) sleep and a marked increase in REM latency. During the followup period, the good response group was also distinguishable not only by clinical response, but by the fact that they experienced more sleep time than the poor response group. Findings partially support Fawcett's work, which showed that the dextroamphetamine response was a possible predictor of improvement with tricyclic treatment in depression. It was felt that, while the value of sleep parameters as predictors of clinical response requires further exploration,

findings suggest the applicability of such objective measurements. (Journal abstract modified)

224833 Dorus, Elizabeth; Pandey, Ghanshayam N.; Davis, John M.; Dekirmenjian, Haroutune. Illinois State Psychiatric Institute, Chicago, IL **Genetic control of lithium ion distribution.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 167).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, a paper was presented reporting results of studies for genetic control of lithium ion distribution. To confirm such control of lithium (Li) distribution across the red blood cell (RBC) in vivo, five monozygotic and five dizygotic twin pairs were given 300mg of lithium carbonate b.i.d. for 7 days, during which time RBC and plasma Li concentrations were assessed. Findings indicated that interindividual variation in blood levels of Li in manic-depressive patients may be related to genetic control of Li transport. Of particular clinical interest was the RBC Li/plasma Li ratio concentration, which other researchers have suggested is higher in manic-depressives than in normal controls, and higher in Li responders than in nonresponders. The possibility is raised that genetically controlled cell membrane properties may be important in the understanding of manic-depressive illness. (Journal abstract modified)

224834 Asberg, Marie. Department of Psychiatry, Karolinska Sjukhuset, Stockholm, Sweden **Nortriptyline plasma levels: relationship to drug effects.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 168-169).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, a paper was presented reporting studies of the relationship between plasma levels of the tricyclic antidepresant nortriptyline and the biological effects of this drug in depressed patients. It was noted that the metabolic clearance rate and the plasma level of nortriptyline during chronic administration varies considerably between patients, but remains constant in a given patient unless dosage is changed or other drugs are given. The concentration of nortriptyline in plasma is strongly correlated to the inhibition of monamine uptake in vivo and in vitro. There is also a correlation between nortriptyline plasma level and a central drug effect. The relationship between plasma level and antidepressant effect appears more complex. It was noted, in treatment, that outcome was more favorable on intermediate plasma levels than on lower and higher levels. It was concluded that nortriptyline plasma level analyses may be useful to reveal errors in drug compliance and to establish the cause of side-effects. (Journal abstract modified)

224835 Kragh-Sorensen, Per; Baastrup, Poul Christian; Hansen, Christian Eggert; Hvidberg, Eigill F. Department O, State Mental Hospital of Glostrup, Copenhagen, Denmark **Dose response relationship for nortriptyline in endogenous depression.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 169-170).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, a paper was presented reporting data on the significance of plasma concentration measurements of nortriptyline (NT) and the relationship of these concentrations to the therapeutic effects of the drug. Results of a triple-blind study of 24 patients suffering from moderate to severe endogenous depression confirmed those of other research which reported that this relationship was unusual. Therefore, strong evidence was established for the assumption that high plasma concentrations of NT lead to a decreased therapeutic effect in patients suffering from endogenous depression. The best therapeutic results were obtained on a plasma level ranging from 50-150ng NT/ml. (Journal abstract modified)

224836 Glassman, Alexander; Perel, James M.; Shostak, Michael; Kantor, Shepard J.; Fleiss, Joseph L. Affective Disease Unit, Dept. of Biological Psychiatry, New York State Psychiatric Institute, New York, NY **Plasma level, depressive typology, clinical outcome.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 170-171).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, a paper was presented reporting results of studies of the relationship between plasma levels of impramine, desmethylimipramine and clinical outcome. Seriously depressed patients free of schizophrenia, organic brain disease, or significant medical illness were used. If these depressed patients were exmained without regard to subtype, no relationship was obtained between plasma level and clinical outcome. However, if subgroups within the depressive population were examined, significant relationships occurred. Patients were divided into bipolar and unipolar groups, with focus on the unipolar group. Clinical data suggested that nondelusional depressives responded well, but that delusional depressives responded poorly to tricyclic therapy. This difference was significant at the 0.05 lvel. If the delusional depressive were excluded and the nondelusional depressive examined separately a significant relationship between the plasma level of imipramine and clinical outcome was obtained. This interrelationship between depressive typology, plasma level of antidepressant, and clinical outcome was discussed in detail. (Journal abstract modified)

224871 Mendels, Joe. Department of Psychiatry, University of Pennsylvania, Philadelphia, PA **Lithium in the treatment of depression.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 213-214).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, a paper was presented in which data from studies of the use of lithium (Li) in treating depression were reported. Studies show that any antidepressant effect which lithium might exert only occurs in a specific subgroup of patients. Depressive patients who respond to lithium treatment differ from other depressives in significant ways: (1) they are more likely to suffer from a manic-depressive (bipolar) illness than from a unipolar illness; (2) they have a significantly higher erythrocyte (RBC) lithium concentration and RBC Li:plasma/lithium ratio. The difference is not a function of dose or plasma lithium concentration. Manic-depressives also have a proportionately higher RBC lithium concentration than controls. Genetic factors may play an important role in the determination of RBC lithium concentration. These and other findings suggest that the subgroup of patients who respond to lithium may have a genetically determined abnormality in some aspect of cell membrane properties which regulate the movement of lithium. Finally, they may have significantly lower platelet monoamine oxidase activity than nonresponders. (Journal abstract modified)

224872 Prien, Robert F.; Caffey, Eugene M., Jr. Central Neuropsychiatric Research Laboratory, Veterans Administration Hospital, Perry Point, MD **Relationship between dosage and response to lithium prophylaxis in recurrent depression.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 214).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, the results of a multihospital collaborative study on the effectiveness of lithium prophylaxis in recurrent depression were reported. It was found that serum lithium levels between 0.5and 0.7milliequivalents per liter and doses below 1,000mg per day were relatively ineffective in preventing recurrences. Serum levels between 0.8and 1.0milliequivalents per liter and doses above 1,000mg per day were associated with a relatively low rate of failure. Implications of findings were discussed, particularly as they pertain to current prescription guidelines for lithium carbonate. (Journal abstract modified)

224873 Dunner, David L.; Fleiss, Joseph L.; Fieve, Ronald R. Department of Internal Medicine, New York State Psychiatric Institute, New York, NY **Lithium carbonate prophylaxis failure.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatriac Assn., 1975. 354 p. (p. 215-216).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, a paper was presented reporting the clinical course of 103 bipolar manic-depressive patients treated at a lithium clinic. All patients had been previously hospitalized on at least one occasion for a manic episode and were well for at least 4 weeks during followup. Failure episodes were determined by reviewing the patients' records, and were defined by symptoms of depression or mania which led to prescription of additional medication or duration of these symptoms for at least 4 weeks. The life table for patients not treated with lithium carbonate revealed a significantly higher rate of failure compared to lithium treatment, confirming earlier reports. For lithium patients, two components were related to probability of failure. There is an initial rate of failure within the first 4 to 6 months. After this time period, the rate of failure was low and almost exponential with time. Clinical factors in the 2 year period prior to treatment did not differentiate patients who failed early from those who failed late or remained well. However, patients who had an early failure were more apt to have a second one. (Journal abstract modified)

224874 Fieve, Ronald R.; Dunner, David L.; Stallone, Frank; Kumbaraci, Turkan; Fleiss, Joseph. Lithium Clinic and Metabolic Unit, New York State Psychiatric Institute, New York, NY **Lithium prophylaxis of three depression sub-types.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 216-217).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, a paper was presented in which lithium prophylaxis in three depression subtypes was described. It was found that lithium reduced both the frequency and severity of recurrent unipolar depressions as compared to placebo; the percent of time in well interval phases was greater, and frequency of hospitalization was greatly reduced. Treatment of bipolar manic-depressives indicated the comparative effectiveness of lithium over placebo in the prophylaxis when frequency of attacks were analyzed. The fact that fresh bipolar depression cases on lithium do not demonstrate depression prophylaxis early is supported by life curves that demonstrate prophylaxis of depressive attacks although attenuation of severity of depression was noted. (Journal abstract modified)

225063 Smith, Ronald C. Dept. of Psychiatry, University of Southern California, School of Medicine, Los Angeles, CA **Amoxapine, imipramine and placebo in depressive illness.** Current Therapeutic Research. 18(2):346-353, 1975.

A 6 week, double-blind study was designed to compare amoxapine with imipramine and placebo with respect to therapeutic efficacy and side-effects. Ninety depressed outpatients who met specified selection criteria were randomly allocated to each of the three treatments to provide 30 patients in each treatment group. Hamilton Depression Scale findings show amoxapine to be superior to placebo in alleviating sleep disturbances as well as anxiety and depression after one to two weeks of therapy; imipramine was more effective than placebo in reducing agitation. Self Rating Symptom Scale results favor amoxapine over placebo in the reduction of general depression and agitation, and amoxapine over imipramine in improving appetite; imipramine produced a greater decrease in irritability and restlessness than placebo. It is concluded that amoxapine at a daily dosage of 600mg is an effective agent for the treatment of depressive disorders in outpatients. Level of efficacy appears at least equal and perhaps superior to that of imipramine at daily dosage of 150mg. Side-effects produced by both drugs appeared to be similar in type, incidence and severity. 7 references. (Author abstract modified)

225086 Okuma, Teruo; Kishimoto, Akira; Inoue, Kinuo; Ogura, Chikara; Motoike, Mitsuo; Matsushima, Yoshihiko; Nakamura, Kazuyasu; Tanaka, Kiyoshi. Dept. of Psychiatry, Tohoku University School of Medicine, Japan **Antimanic and prophylactic effects of carbamazepine (Tegreto) on manic depressive psychosis.** Clinical Psychiatry (Tokyo). 17(6):617-630, 1975.

The antimanic, antidepressive, and prophylactic effects of carbamazepine (CAZP, Tegreto-l) were investigated in 90 endogenous manic-depressive psychotics (MDP). The dosage of the drug ranged from 200 to 1200mg daily (usually 400 to 600mg). Findings indicate that CAZP was effective in 35 manic patients and ineffective in 30. CAZP was effective in three cases of depression and ineffective in six. No definite relationship was found between the drugs used in combination with CAZP and the effect of CAZP. No significant difference in the CAZP effect was found in the four patient groups with different ages of onset of the illness, nor among the "continuous," "frequent," and "periodic" type of cases. The prophylactic effect of CAZP on 51 cases was positive in 34 cases and it was ineffective in 17; for depressive episode it was effective in 27 cases and ineffective in 15. The prophylactic effect of CAZP was more marked in chronic cases with early onset. 21 references. (Journal abstract modified)

225107 Murphy, J. E. Northampton, England **A comparative clinical trial of Org GB 94 and imipramine in the treatment of depression in general practice.** Journal of International Medical Research (Northampton). 3(4):251-260, 1975.

A double-blind controlled comparative clinical trial of Org-GB-94 and imipramine was conducted in general practice. Fifty five patients were treated with Org-GB-94 (60mg daily) and 54 with imipramine (150mg daily). In the doses employed, both agents were equally effective in relieving depression over a 4 week treatment period. Tolerance of the two agents was

similar. Although no statistically significant differences emerged with regard to both therapeutic effect and some side-effects, a trend in favor of Org-GB-94 was apparent. 14 references. (Author abstract)

225386 Woody, George E.; O'Brien, Chalres P.; Rickels, Karl. Veterans Administration Hospital, University and Woodland Ave., Philadelphia, PA 19104 **Depression and anxiety in heroin addicts: a placebo-controlled study of doxepin in combination with methadone.** American Journal of Psychiatry. 132(4):447-450, 1975.

A placebo - controlled study was designed to test the hypothesis that heroin addicts in methadone treatment program with ratable depressive symptomatology should show more improvement when treated with doxepin than with placebo. It is indicated that narcotic addicts may manifest symptoms of depression that aggravate their addiction. In this double-blind study of 35 midly depressed patients in a methadone maintenance program, subjects who receive doxepin improved significantly more than control subjects. It is shown that the reduction in depression is associated with a trend toward better performance in other areas of rehabilitation. 11 references. (Journal abstract modified)

225512 Fisher, Dorrice; DiMino, Joseph M. no address **Case presentation of an alternative therapuetic approach for the borderline psychotic heroin addict: diphenylhydantoin.** British Journal of Addiction (London). 70:51-55, 1975.

The use of diphenylhydantoin (DPH) to stabilize hyperexcitable nerve cells and tissues in the postsynaptic membranes, combined with a type of cognitive therapy is examined as treatment for a borderline psychotic heroin addict. In a case history, the heroin addict, who was a borderline psychotic with possible brain damage, improved with the use of DPH and special ego oriented cognitive therapy as long as he remained on DPH. This same regimen was used with 36 other patients who exhibited similar encouraging results. 12 references.

10 DRUG TRIALS IN NEUROSES

214829 Capstick, N. Graylingwell Hospital, Chicester, Sussex, England **The Shapiro Cards Scale as a method of assessment of obsessional symptoms in clomipramine therapy.** Scottish Medical Journal (Glasgow). 20(Suppl. 1):17-20, 1975.

A method of rating obsessional symptoms is described. The technique was devised by Shapiro and is directed toward overcoming two major problems encountered in research into the value of new treatment for obsessional states: the small number of patients seen in any one center and the great diversity of symptoms which obsessional patients display. The application of the technique to the treatment of obsessional disorders is illustrated. 2 references. (Author abstract modified)

214833 Allen, J. J.; Rack, P. H. Lynfield Mount Hospital, Bradford, England **Changes in obsessive/compulsive patients as measured by the Leyton Inventory before and after treatment with clomipramine.** Scottish Medical Journal (Glasgow). 20(Suppl. 1):41-44, 1975.

The Leyton Obsessional Inventory was found to be a useful measure in assessing patients before and after treatment with clomipramine. Mean scores for symptoms and interference altered significantly during the course of treatment. The Inventory, however, lacks external validation owing to the absence of some valid alternative quantification. In the absence of such external validation, it is recommended that the mean Leyton score be used diagnostically, but not as a sole indication of severity or response to treatment. 5 references. (Author abstract)

214835 Marshall, W. K.; Micev, V. Severalls Hospital, Colchester, England **The role of intravenous clomipramine in the treatment of obsessional and phobic disorders.** Scottish Medical Journal (Glasgow). 20(Suppl. 1):49-53, 1975.

The results of intravenous clomipramine therapy in 118 patients suffering from obsessional syndromes and phobic anxiety states are reviewed. A remarkable consistency of improvement was observed, especially in those patients suffering from obsessional symptoms. Better results were obtained in patients lacking hysterical personality traits. A brief reference is made to a pilot study involving the use of the 16 Personality Factor test in assessing the effect of clomipramine. 2 references. (Author abstract)

214836 Colgan, Anthony. Cluain Mhuire Family Centre, Dublin, Ireland **A pilot study of Anafranil in the treatment of phobic states.** Scottish Medical Journal (Glasgow). 20(Suppl. 1):55-60, 1975.

A pilot study of the use of Anafranil in the treatment of phobic disorders is described. Twenty two patients were included, 16 receiving intravenous and oral Anafranil combined and six receiving oral Anafranil alone. After 1 month, four were free of phobic symptoms and 13 were only mildly disabled. At 6 month followup, 10 were free of symptoms and seven only mildly disabled. 5 references. (Author abstract)

214837 Waxman, D. Central Middlesex Hospital, London **An investigation into the use of Anafranil in phobic and obsessional disorders.** Scottish Medical Journal (Glasgow). 20(Suppl. 1):61-66, 1975.

A multicenter clinical trial of clomipramine in the treatment of obsessional and phobic disorders in general practice is described. All phobias showed an improvement in situational anxiety, interference and autonomic side-effects. With the exception of two cases of animal phobia, there was also improvement in general anxiety and avoidance. Obsessional cases showed an overall improvement in all symptom areas. 8 references. (Author abstract)

214838 Wootton, L. W.; Bailey, R. I. Swanley, Kent, England **A preliminary report on the use of clomipramine in general practice.** Scottish Medical Journal (Glasgow). 20(Suppl. 1):67-71,, 1975.

The use of clomipramine in a large suburban general practice is reviewed. Out of a total practice population of 21,000, 350 patients were treated with this drug. Phobic anxiety states appear much more common than is normally supposed and are usually associated with a history of separation or rejection in childhood. It is noted that side-effects of clomipramine treatment may initially present a problem, though they may not be truly drug induced. Case illustrations are included to illustrate some of the impressive results that have been obtained with this therapy. (Author abstract modified)

215060 Schiff, A. A.; Murphy, J. E.; Anderson, J. A. E. R. Squibb and Sons, Ltd., Twickenham, Middlesex, England **Non-pharmacological factors in drug therapy--the inter-action of doctor, patient, and tablet appearance in the treatment of anxiety/depressive syndromes.** Journal of International Medical Research (Cambridge). 3(2):125-133, 1975.

The degree to which placebo response is involved in an active treatment situation in normal clinical practice, and the factors comprising the placebo response were analyzed in a study on patients with anxiety - depressive syndromes. Four tablet preparations of different appearance but identical pharmacological activity were used over a 3 week period and a comparison of therapeutic benefits between treatments doctors, and doctor-patient groupings was made, in addition to an analysis of the relationship of patients' self-assessment with their physicians' drugs. Results indicate that, although direct pharmacological effect was paramount in determining therapeutic outcome, detailed differences were related to various placebo factors. The similarity between physicians' and patients' rating tends to decrease during the course of treatment, and possible reasons for this are reviewed in light of previous research. 14 references. (Author abstract modified)

215061 Roubi, A. El. Cairo University, Cairo, Egypt **Lorazepam in the management of gastro-intestinal neuroses.** Journal of International Medical Research (Cambridge). 3(2):134-137, 1975.

The use of lorazepam in the management of gastrointestinal neuroses was investigated. Thirty seven patients showing objective evidence of psychosomatic symptoms or gastrointestinal neuroses were given lorazapam for 3 weeks. Response, measured weekly by the Hamilton Rating Scale for anxiety, showed that 23 patients were much improved, 11 were moderately improved and three were slightly improved. The improvement between pretreatment assessment and final rating was significant. Side-effects were mild and transient. 18 references. (Author abstract modified)

215152 Murphy, J. E. Northampton, England **Comparative studies with clomipramine (Anafranil) and clomipramine combinations.** Journal of International Medical Research (Cambridge). 3(Suppl.1):63-71, 1975.

The use of combinations of anxidytic and antidepressant drugs in patients suffering from psychiatric disorders with features of both anxiety and depression was examined. Two clinical studies are reported in which a combination of Insidon and Anafranil was compared with Limbitrol 10 and in which a combination of Insidon and low dose Anafranil was compared with Anafranil itself. Findings indicate that the Insidon/Anafranil combination appeared superior to Limbitrol 10 though not significantly so. Results reveal that the Insidon/Anafranil combination was superior to Anafranil in the relief of anxiety but the higher dosage of Anafranil was superior to the combination in the relief of depression. 8 references. (Author abstract)

215155 Capstick, N. Graylingwell Hospital, Chichester, Sussex, England **Clomipramine (Anafranil) in the treatment of obsessional states: a psychiatrist's view.** Journal of International Medical Research (Cambridge). 3(Suppl.1):83-88, 1975.

The definition, classification and incidence of obsessional disorders is briefly discussed. Some aspects of the psychopathology of obsessionality are considered. Methods of treatment, particularly involving the use of clomipramine, are described. As clomipramine is a powerful antiobsessional drug, the removal of obsessions may be a drastic procedure and careful rehabilitation is required. The treatment of the obsessional patient could be a fruitful field for cooperation between the general practitioner and the psychiatrist. 7 references. (Author abstract)

215156 Marshall, W. K. Severalls Hospital, Colchester, England **Clomipramine (Anafranil) in the treatment of phobic states: a psychiatrist's view.** Journal of International Medical Research (Cambridge). 3(Suppl.1):89-93, 1975.

The manner of presentation of phobic anxiety states is described and the frequency of various types of disorder considered. Available methods of treatment are reviewed. Clomipramine, especially by intravenous infusion, is the preferred method. Results of treatment are given and some aspects of management discussed. (Author abstract)

215157 Waxman, D. Dept. of Psychological Medicine, Central Middlesex Hospital, London, England **A general practitioner trial of clomipramine (Anafranil) in obsessions and phobias.** Journal of International Medical Research (Cambridge). 3(Suppl.1):94-100, 1975.

A multicenter open clinical trial of clomipramine (Anafranil) in obsessional and phobic disorders was performed in general practice. Sixteen doctors contributed 32 patients. Twenty seven patients completed 6 weeks' treatment on doses as high as 225mg daily. Findings indicate that all phobics showed improvement in situational anxiety, interference and autonomic effects. All but two phobics, suffering from animal phobias, showed improvement in general anxiety and avoidance. Obsessionals improved on every parameter assessed. 9 references. (Author abstract)

215158 Wootton, L. W.; Bailey, R. I. Swanley, Kent, England **Experiences with clomipramine (Anafranil) in the treatment of the phobic anxiety states in general practice.** Journal of International Medical Research (Cambridge). 3(Suppl.1):101-107, 1975.

Experiences with clomipramine (Anafranil) in the treatment of the phobic anxiety states in general practice are reviewed. It is noted that phobic disorders are frequently encountered in general practice and may present in a number of guises. They have a common etiology and invariably are associated with rejection, actual or apparent, usually in the middle childhood years. Anafranil is considered mandatory treatment. During the first month it is given with Prothiaden and propranolol in order to counteract unwanted effects. Thereafter it is used alone, treatment lasting at least 9 months. Some illustrative case histories are provided. (Author abstract)

215694 Poldinger, W. Chefarzt, Kant. Psychiatrische Klinik, 9500 Wil/SG, Switzerland **Clinical trial of 3-methyl-5-(beta-N'-(N-m-chlorophenylpiperazino)ethyl)-pyraz zole dihydrochloride (Mepiprazol) in the therapy of psychovegetative disorders.** International Pharmacopsychiatry (Basel). 10(1):1-8, 1975.

In a clinical trial of 30 patients suffering from psychovegetative disorders and anxiety neuroses, Mepiprazol was proven in a treatment period of 14 days to be an effective, well tolerated medication. Only two patients failed to respond during the course of treatment. Improvements were significant at the 1% level between the pretreatment condition and each control during the treatment period; even between the rating times there was a significant increment in treatment success. Mepiprazol had a particular effect on symptoms such as irritability, anxiety, inner unrest and tension. Mepiprazol also exhibited a positive effect in the treatment of psychosomatic complaints. 10 references. (Author abstract)

216335 Denber, Herman C. B. Dept. of Psychiatry, School of Medicine, University of Louisville, Louisville, KY **Pharmacotherapy of depressions.** Current Psychiatric Therapies. 14:135-146, 1974.

The question of the correct use of drugs in treating neuroses and the correct diagnosis of various neuroses is addressed. General rules for treatment with antidepressants are noted: diagnosis must be certain; lower dose ranges should be used at first; medication should be kept constant, for at least 1 week; reduce dosage slowly; and correct use of maintenance medication. Further discussion is provided, concerning monoamine oxidase inhibitors, the tricyclic drugs, antianxiety drugs, lithium, electroconvulsive therapy, phenothiazines and milieu manipulation. It is indicated that one of the most important therapeutic processes is careful continuous monitoring of progress from the outset. 51 references.

216462 Rickels, K.; Case, W.; Csanalosi, I.; Pereira-Ogan, J. A.; Parish, L.; Bell, P. J. no address **Lorazepam in anxiety: a controlled study.** Journal of International Medical Research (North Hampton). 2:20-25, 1974.

Lorazepam (3mg/day) was compared to a placebo in a double-blind study with anxious neurotic patients. Sixty eight patients were treated for a least 2 weeks. The most significant therapeutic effect was found in patients taking lorazepam. Nevertheless, this produced greater improvement than the placebo in evaluations by the physician rather than by the patient. Lorazepam seemed more effective with patients who were more ill at the beginning of the trial. Its principal side-effect is sedation of vigilance.

217455 Sonne, Lass Mahler; Holm, Per. Augustenborg Mental Hospital, DK-6440 Augustenborg, Denmark **A comparison between bromazepam (Ro 5-3350, Lexotan) and diazepam (Valium) in anxiety neurosis: a controlled, double-blind clinical trial.** International Pharmacopsychiatry (Basel). 10(2):125-128, 1975.

The new benzodiazepine bromazepam (Ro 5-3350, Lexotan) was compared with diazepam in a double-blind, crossover trial on 30 patients with prolonged anxiety symptoms. Each drug was given for 3 weeks in a dose of 5mg t.d.s. Bromazepam proved to be statistically significantly superior to diazepam when evaluated through patients' preferences. Fourteen patients preferred bromazepam to diazepam and four the opposite. Three cases were tied. Nine patients had to be withdrawn from the evaluation, which may create bias. A plea is made for further controlled clinical trials on bromazepam, in particular in obsessive and phobic neurosis. 4 references. (Author abstract)

217460 Tansella, M.; Siciliani, O.; Barti, L.; Schiavon, M.; Tansella, Ch. Zimmerman; Gerna, M.; Tognoni G.; Morselli, P. L. Istituto di Clinica Psichiatrica di Verona, Universita di Padova I-37100 Verona, Italy **N-desmethyldiazepam and amylobarbitone sodium as hypnotics in anxious patients. Plasma levels, clinical efficacy and residual effects.** Psychopharmacologia (Berlin). 41(2):81-85, 1975.

Drug plasma levels of N-desmethyldiazepam (10 and 20mg/day given at night) and amylobarbitone sodium (200mg/day given at night) were determined in 45 patients after 1 and 7 days of treatment together with estimates of hypnotic and residual effects. No relationships were found between clinical ratings of hypnotic effect and drug plasma levels, while significant correlations were observed between some performance tasks and drug plasma concentrations of amylobarbitone sodium, and of the higher dose of N-desmethyldiazepam. 19 references. (Author abstract)

218750 Deberdt, R. Poperingeweg 10, B-8900 Ieper, Belgium **A multicentric evaluation of pimozide (Orap) in patients who usually would take tranquillizers.** Acta Psychiatrica Belgica (Bruxelles). 74(6):653-660, 1974.

Pimozide (Orap) was administered to 53 outpatients requiring tranquilizers in an 8 week trial with 2mg daily doses. The patient's condition was assessed by means of the Hamilton Anxiety Rating Scale. All items on the questionnaire showed significant improvement, although insomnia and anxiety decreased less than the other items. A significant improvement of socioprofessional adaptation was also found. It is concluded that patients who would usually take tranquilizers are suitable candidates for pimozide treatment. It is recommended that patients manifesting marked anxiety and/or insomnia be treated with both a tranquilizer and pimozide. 13 references. (Journal abstract modified)

218769 Friedman, Alfred S. Philadelphia Psychiatric Center, Ford Road and Monument Avenue, Philadelphia, PA 19131 **Interaction of drug therapy with marital therapy in depressive patients.** Archives of General Psychiatry. 32(5):619-637, 1975.

Comparative effects of amitriptyline hydrochloride, marital therapy, and the drug - psychotherapy interaction effects were studied in a 12 week course of treatment of outpatient neurotic depressives. Patients were assigned randomly to four treatment groups: drug - marital therapy, drug - minimal contact, placebo - marital therapy, and placebo - minimal contact. Both drug and marital therapy showed substantial advantages over their control conditions, but drug therapy was faster and generally superior in symptom relief and clinical improvement. Marital therapy was superior in family role task performance and perception of the marital relationship. For reducing hostility and enhancing the perception of the marital relationship, drug therapy had a better early effect but marital therapy had superior effects by the end of treatment. 28 references. (Author abstract modified)

218771 Wheatley, David. General Practitioner Research Group, 325 Staines Rd., Twickenham, TW2 5AX, England An **adrenergic drug in depression.** Archives of General Psychiatry. 32(5):653-655, 1975.

A unique clinical investigation into a beta-adrenergic stimulant for the treatment of mild depression in 44 patients is reported. The adrenergic drug metaproterenol sulfate was combined with chlordiazepoxide hydrochloride and compared to placebo and chlordiazepoxide in a formal double-blind trial. However, the results did not show any advantage for the addition of metaproterenol either in respect to enhanced antidepressant effect or reduced incidence, nature, or severity of side-effects. 17 references. (Author abstract modified)

221035 Pelc, I. Universite Libre de Bruxelles, Institut de Psychiatrie, Hopital Brugmann, 4 Place Van Gehuchten, B 1020 Brussels, Belgium **Doxepin i.m. in the treatment of depression and anxiety.** Current Therapeutic Research. 17(5):467-477, 1975.

The antidepressant and anxiolytic activity of doxepin (Sinequan) administered intramuscularly to depressive - anxious patients was evaluated in a group of 30 inpatients. After a 6 day treatment, the biphasic activity of the drug was already evident; improvement in the depressive state, mood, and anxiety (Hamilton depression scale) was approximately 50%. No significant differences were found between doxepin and amitryptyline, although doxepin tends to cause fewer side-effects. Results show that changes in mood and anxiety levels were parallel during the first 6 days of treatment, suggesting that these variables are closely linked in the depression - anx-

iety states and raising the question of how to grade them in psychopharmacological trials. 11 references. (Author abstract modified)

221269 Cesa-Bianchi, M.; Ghirardi, P.; Ravaccia, F. Istituto di Psicologia della Facolta Medica, Universita di Milano, Milan **A preliminary double-blind study with SB 5833 (camazepam), a new benzodiazepine derivative.** Arzneimittel-Forschung (Aulendorf). 24(1):2032-2035, 1974.

A new benzodiazepine derivative, 3-N-N-dimethylcarbamoyloxy-7- chloro-5-phenyl-1-methyl-1,3-dihydro-2H-1,4-benzodiazepine-2-one (SB 5833, camazepam) was compared with temazepam in a double-blind clinical trial performed on psychoneurotic patients. The evaluation of mental disorders was made with a very simple self-rating scale 10 items. The results of statistical evaluation are favorable for SB 5833, indicating that the drug significantly improved depressive mood. 13 references. (Journal abstract)

221304 Cassano, G. B.; Carrara, S.; Castrogiovanni, P. Psychiatric Clinic of University of Pisa, Pisa, Italy **Bromazepam versus diazepam in psychoneurotic inpatients.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 8(1):1-7, 1975.

A double-blind, between groups trial was carried out to compare the effectiveness of the new benzodiazepine compound, bromazepam (Lexotan, Ro 5-3350) as an antianxiety compound with that of diazepam. The 58 psychoneurotic inpatients admitted to the trial were divided into obsessive and neurotic groups. Assessment was made by means of the Brief Psychiatric Rating Scale, the Rating Scale for Anxiety States, the Psychiatric Rating Scale, and the Inpatient Multidimensional Psychiatric Scale (IMPS). Results show that bromazepam has a general therapeutic effectiveness as an antianxiety agent. While no difference in the effects of the two drugs was discernible between the two psychopathologic groups, in both treatments the obsessives respond less than the neurotics. Detailed evaluation of the individual items of the IMPS shows that bromazepam is likely to exert a disinhibiting or activating action, unlike most other benzodiazepines in clinical use. 10 references. (Journal abstract)

221337 Bergener, M.; Escher, H. D.; Linden, K. J. Rheinische Landesklinik Koln, Psychiatrisches Behandlungszentrum, 5 Koln 91, Wilhelm-Griesinger-Str. 23, Germany **/The significance of standardized evaluation scales in psychiatric diagnosis as exemplified by the therapeutic intervention with desmethyl-loxapine./** Die Bedeutung standardisierter Beurteilungsskalen in der psychiatrischen Diagnostik -- dargestellt am Beispiel eines Therapieversuchs mit Desmethyl-Loxapin. Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 8(2):69-81, 1975.

The advantages and disadvantages of standardized rating scales in psychiatric diagnosis are discussed. It is concluded that these instruments at present are irreplaceable in psychopathological research because of their reliability in transmitting information and the possibility of quantifying psychopathological syndromes. The use of four rating scales little known within German speaking countries is demonstrated by means of a psychopharmacological investigation of the clinical effects of desmethyl-loxapine. These rating scales are: 1) the Hamilton Psychiatric Rating Scale for Depression, 2) the Wittenborn Psychiatric Rating Scale, 3) the Structured Clinical Interview, and 4) the Befindlichkeits Skala (Condition Scale). Desmethyl loxapine was given in an open study as an antidepressant to 16 patients with different depressive syndromes. The results of the 3 to 4 week treatment are discussed. The therapeutic efficacy of desmethyl-loxapine is attributed to its marked anxiolytic effect and excellent tolerance. 14 references. (Journal abstract modified)

221638 Beck-Friis, Johan; Fyro, Bengt; Sjostrand, Inga-Greta. Psykiatriska kliniken, S:t. Gorans sjukhus, 112 81 Stockholm **/A comparison between diazepam and haloperidol in neurotic anxiety and tension states in patients in a open ward./** En jamforelse mellan diazepam och haloperidol vid neurotiska angest- och spanningstillstand hos patienter i oppen vard. Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(6):465-467, 1974.

In a double-blind cross-over experiment comparing diazepam, a common minor tranquilizer, with the major tranquilizer haloperidol, diazepam was found to be more effective than haloperidol in the symptomatic treatment of 51 patients with neurotic anxiety and tension states. Patients were divided into two groups: those with anxiety not attributable to a conscious cause, and those with anxiety attributable to a conscious source. Diazepam was significantly more effective in the first group; there was no significant difference between diazepam and haloperidol in the second group in therapeutic effect. Haloperidol may be recommended in the treatment of the second group, as it has few side-effects and minimal potential for the increase in tolerance and physical dependence often ascribed to diazepam use. 10 references.

221891 Ruangtrakool, Sompop; Thongstang, Orapan. Department of Psychiatry, Faculty of Medicine, Siriraj Hospital, Mahidal University, Bangkok, Thailand **Mild depressive illness.** Journal of the Medical Association of Thailand (Bangkok). 57(11):558-563, 1974.

Symptoms of mild depressive illness commonly encountered in medical practice are discussed. The most important symptoms are fatigue, anorexia and weight loss, insomnia, depressed mood, loss of interests and sexual desire, feeling of unworthiness, and death wishes. Although diagnosis of this mild form of depression may be difficult, early detection is possible if the physician is aware of the symptomatology of this mild form of depression, particularly in patients over age 30. Two case histories are presented in which the patients were successfully treated with amitriptyline (Laroxyl). 4 references. (Author abstract modified)

222772 Braun, Judith; Jimerson, David; Morrison, James. University of California at San Diego School of Medicine, La Jolla, CA 92037 **Anxiety neurosis, depressive disorder and meprobamate addiction -- Psychiatric Grand Rounds, Univ. of California, San Diego** Western Journal of Medicine. 123(2):115-122, 1975.

A case study of a middle-aged mother of eight who had been on meprobamate for 4 years was evaluated by a group of psychiatrists. An edited analysis of her psychotherapy and a detailed segment of an interview between patient and psychoanalyst are presented. The woman had been depressed following her sterilization some years earlier, and had been taking meprobamate (Equanil) for several years. Contributions from a panel of doctors concerning the progress in the patient's therapy are also included. 9 references.

223182 Okada, Michio; Takei, Hiroshi; Haga, Michinobu; Kato, Tomoyuki. Laboratory of Cranial Nerves, Kanto Teishin Hospitaal, Higashi Gotanda, Shinagawa-Ku, Tokyo **On the antidepressant effect of CIBA 34276 Ba (Maprotiline).** Japanese Journal of Clinical Psychiatry (Tokyo). 3(10):1105-1114, 1974.

The effectiveness of Maprotiline as an antidepressant was studied in 32 depressed patients. Ss were administered 50-150mg daily for 6 weeks, with the majority showing good to excellent results. Dryness of the mouth and sleepiness were the most prevalent side-effects, but with continued, controlled use of the medication, these symptoms disappeared. Two successful case studies are included. 11 references.

224194 Ueno, Fumiya; Otsuka, Kensei; Nakanishi, Shigeo; Honda, Kosaku. Department of Neuropsychiatry, Fukushima Medical College, Fukushima, Japan **Clinical trails of sulpiride with emphasis on neurotic outpatients.** Clinical Consultation & New Remedies (Tokyo). 11(10):2175-2186, 1974.

The effect of sulpiride on neurosis was studied in an experiment in which 20 patients with neurosis and 7 patients with depression, schizophrenia and arteriosclerosis were orally treated with this drug (100-400mg/day) for 7-401 days. Sulpiride was effective to some extent in all but one of the neurotics and in half of the entire group. Minor side-effects were observed in seven patients, but only in one case did they require treatment. 18 references.

224583 De Geyter, J.; Dumont, E.; Stenier, P. Clinique neurologique de la Ramee, 27, rue de la Ramee, 1180 Brussels, Belgium **/Clinical study of a new tranquilizer, Lexotan, in neurotic disturbances./** Etude clinique d'un nouveau tranquillisant, le Lexotan, dans les troubles nevrotiques. Semaine des Hopitaux Therapeutique (Paris). 51(4):247-252, 1975.

A clinical study was made of a new tranquilizer, bromazepam (Lexotan), with a patient population suffering from neurotic disturbances. Bromazepam was found to be more effective than diazepam (Valium), especially in strongly structured neuroses such as obsessional and phobic neuroses. In a double-blind study, bromazepam acted somewhat better than diazepam with obsessional neuroses, but the difference in effect was not statistically significant. Both drugs had a similar effect; the average daily dose was 10mg for bromazepam and 11mg for diazepam. Side-effects were similar for the two drugs, including somnolence and adynamia. 16 references.

224767 Covi, Lino; Lipman, Ronald S.; Guzman, Renato Alarcon. Johns Hopkins Hospital, Baltimore, MD **Drug psychotherapy interactions in depression.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 89-90).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, May 1975, a paper was presented which discussed the statistically significant interactions and main effects of group psychotherapy and pharmacotherapy in chronic neurotic depression. Data from 200 female outpatients indicate that main effects favoring group psychotherapy occurred early in treatment on measures of mood, and were evident later in therapy in ratings reflecting the relationship between patient and husband or another significant person. On many measures of mood and neurotic symptomatology (anxiety), a drug by psychotherapy interaction, and in some cases a multiple interaction (with social class or clinic), was found. Although differences among three medication groups were most pronounced under minimal psychotherapy conditions, imipramine effected the most improvement, followed by placebo and diazepam in minimum and maximum therapy conditions. Group therapy patients were better able to adjust to the minimal contact and no medication during the maintenance year than were minimal therapy patients requiring active medication. Drug effects favoring imipramine were very strong. (Journal abstract modified)

224984 Munjack, Dennis J. Adult Outpatient Psychiatry Clinic, 1237 North Mission Road, Los Angeles, CA 90033 **Overcoming obstacles to desensitization using in vivo stimuli and Brevital.** Behavior Therapy. 6(4):543-546, 1975.

The use of methohexital (Brevital) to overcome resistance to systematic desensitization is demonstrated. Using intravenous Brevital and real life stimuli in the therapy, a female with multiple phobias showed substantial improvement within 10 sessions. Gradual withdrawal of the drug during prolonged exposure facilitated transfer of the medication's antianxiety effects to the nondrug state. The patient remained improved at 18 month followup. A psychological test battery administered before treatment and at followup substantiated the durability of improvement. 21 references. (Author abstract modified)

225064 Teja, Jagdish S.; Shah, Dinesh K.; Wig, Narendra N. University of Virginia School of Medicine, Charlottesville, VA 22901 **Benzoctamine (Tacitin) versus placebo: a double-blind cross over study in anxiety neurotics.** Current Therapeutic Research 18(2):354-358, 1975.

Benzoctamine (Tacitin), a new antianxiety agent, was compared with a placebo in the treatment of 25 outpatients with anxiety neurosis under double-blind controlled conditions. Benzoctamine was not significantly better than placebo in reducing the total scores on an objective anxiety rating scale, but it had a significant effect on the symptom of anxiety. Placebo produced significantly better results in some patients, which might be due to the fewer number of patients who had side-effects on placebo. 7 references. (Author abstract modified)

225516 Saletu, B.; Saletu, M.; Simeon, J.; Viamontes, G.; Itil, T. M. Psychiatrische Universitatsklinik Wien, Lazarettgasse 14, A-1097 Wien **Comparative symptomatological and evoked potential studies with d-amphetamine, thioridazine, and placebo in hyperkinetic children.** Biological Psychiatry. 10(3):253-275, 1975.

To compare the effects of placebo, thioridazine, and d-amphetmaine on the clinical symptomatology and quantitatively analyzed visual evoked potentials (VEP) in hyperkinetic children, a double-blind experiment was performed. After 8 weeks of treatment with one of the three substances, d-amphetamine was found to be significantly superior to placebo and thioridazine in improving clinical symptomatology. Out of eight symptom clusters rated by the parents, two improved significantly with placebo, one with thioridazine, and six with d-amphetamine. The d-amphetamine was judged superior to placebo in reducing muscular tension and superior to thioridazine in decreasing hyperactive impulsive behavior, psychosomatic problems, and muscular tension. Out of four teachers' symptom clusters, inattentive passive behavior was significantly improved by thioridazine (which was also superior to placebo), while hyperactivity was reduced by d-amphetamine. Quantitative evaluation of VEP revealed an increase in latencies and decrease in amplitudes during thioridazine treatment. Paradoxically, d-amphetamine increased latencies while tending to augment amplitudes. Regression and correlation analysis of clinical symptomatology with VEP variables showed that the shorter the pretreatment latencies and the higher the amplitudes, the more disturbed was the child. During therapy, it was found that the greater the drug induced augmentation of latencies, the greater the clinical improvement. VEP differences between therapy responsive and resistant patients are explored and discussed. 54 references. (Author abstract modified)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

213594 Itil, Turan M. Division of Biological Psychiatry, New York Medical College, New York, NY **New psychotropic drug trials in Turkey.** Psychopharmacology Bulletin. 11(2):5-10, 1975.

Drug trials in Turkey are reported which include clinical studies in patients with anxiety, schizophrenia, or affective disorders, and computer electroencephalogram (CEEG) studies in normal volunteers. The results of trials with amitriptyline, protriptyline, amoxapine, loxapine, clorazepate, phenobarbital, MIF (melanocyte stimulating hormone inhibiting factor), lisuride, cyproterone acetate, and mesterolone in normals; and of trials with TRH (thyrotropin releasing hormone), SA-97, GB-94, GC-94, GC-46, and OI-77 in patient groups are discussed. references.

213614 Heninger, George R. Connecticut Mental Health Center, New Haven, CT **Central neurophysiology of the functional psychoses.** Psychopharmacology Bulletin. 11(2):48-49, 1975.

Electrical measures of brain activity are followed over the period of clinical change during drug treatment in mental patients. The goal is to delineate areas of neurophysiologic functioning associated with symptoms of functional psychosis. Electrophysiological variables which change during therapy or which correlate to symptomatology are further investigated in drug studies on normal subjects and in experiments with laboratory animals. In every manic patient studied, lithium treatment was associated with increased somatosensory evoked response (SER) amplitudes and a reduction in speed of performance on several time performance tests. In most patients, change in SER measurements, EEG theta intensity, and behavioral measures were significantly correlated. Among depressed patients treated with amitriptyline, improvement in symptomatology was related to increased speed of psychomotor performance. In schizophrenic patients, changes in neuroelectrical functioning and psychomotor slowing produced by lithuim were not necessarily associated with alterations in thought disorder.

213786 Avallone, Donna M. Northeastern Univ., Boston, MA **Drug therapy for stutterers: a review of research.** American Archives of Rehabilitation Therapy. 23(1):4-7, 1975.

Research on drug therapy for stutterers is reviewed. Positive effects achieved in early research with drug therapy were also achieved with placebo, suggesting that the effect was primarily psychological. Recent research has concentrated on treatment with haloperidol, but these results have also been of questionable validity. It is concluded that drug therapy for stuttering treats the symptom and not the cause of the problem, and proposed guidelines for evaluating new treatment techniques are outlined. 19 references.

213988 Council on Child Health. no address **Medication for hyperkinetic children.** Pediatrics. 55(4):560-561, 1975.

The use of drug therapy in the management of the hyperkinetic child is discussed. It is felt that there is a place for stimulant drugs in treatment, but that the key factor is proper selection of patients. Since hyperkinesis is rarely an isolated symptom, it is recommended that selection of the drug be based on the patient's medical history and the weighing of risks. Behaviors in which stimulant drugs are effective are described, and agents available, dosage, and side-effects are reviewed. The need to consider nondrug therapy is pointed out. It is concluded that the overall management of school failure is multidisciplinary, and that the physician who is responsible for chemical behavior modification should avail himself of the accumulated knowledge of the subject. 13 references.

214304 Fujii, Kaoru; Nakane, Yoshibumi. School of Medicine, Nagasaki University, Japan **Mental disorders seen after open heart surgery.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(5):485-491, 1974.

Mental disorders seen after open heart surgery in four patients are discussed. A 47-year-old female with valvular disease had right hemisphere incomplete paresis and aphasia and was in a state of shock for 2 days after open heart surgery. Emotional instability, excitation, negativism, and delusion of persecution appeared 50 days after surgery and lasted for 1 month. Chlorpromazine eliminated these symptoms. A 23-year-old female had hallucinations, which completely disappeared after treatment with levomepromazine. A 50-year-old male was in a state of delirium 5 days after surgery, which disappeared after treatment with chlorpromazine. A 50-year-old male had insomnia, general fatigue, loss of appetite, depression, and inhibition in thinking and language 15 days after surgery, which disappeared through treatment with amitriptyline. The first three patients retained a minor case of amnesia. 12 references.

214719 Silverman, Louis B. Grand Forks Clinic, Grand Forks, ND **Orthomolecular treatment in disturbances involving brain function.** Journal of Orthomolecular Psychiatry (Regina). 4(1):71-84, 1975.

History of and rationale for orthomolecular treatment of psychiatric disorders of children and adults are reviewed, and successful treatment of 150 patients with this approach is reported. Results suggest that whenever medical treatment is indicated, the orthomolecular method is the first and safest treatment in children with perceptual and behavioral problems associated with minimal neurological difficulties. Disorders or situations where vitamin therapy is not effective include manic-depressive illness and problems accompanied by severe depression and/or compulsion. 34 references.

215009 Prien, Robert F.; Haber, Paul A.; Caffey, Eugene M., Jr. Central Neuropsychiatric Research Lab., Veterans Administration Hospital, Perry Point, MD 21902 **The use of psychoactive drugs in elderly patients with psychiatric disorders: survey conducted in twelve Veterans Administration hospitals.** Journal of the American Geriatrics Society. 23(3):104-112, 1975.

A survey conducted at 12 Veterans Administration hospitals included the collection of detailed information on the use of psychoactive drugs in 1,276 elderly psychiatric patients. On the day of the survey, 61% of the patients were receiving psychoactive drugs. Prescription practices relating to the choice of drugs, prevalence of drug use, dosage, combination drug preparations, and antiparkinson agents are discussed in terms of such factors as the patient's age and the diagnosis. The literature on psychoactive drugs, particularly as it pertains to elderly populations, is reviewed. 19 references. (Author abstract)

215698 Tacke, B.; Kempf, H. Bergische Landstrasse 2, D-4 Dusseldorf 12, Germany **/On the influence of Aprotinium (Trasylol) in the treatment of alcohol -delirium./** Doppelblindstudie uber aprotininum (Trasylol) in der behandlung des alkoholdelirs. International Pharmacopsychiatry (Basel). 10(1):37-41, 1975.

Continuing a preliminary double-blind study, a group of 20 male patients was examined to evaluate the effectiveness of aprotininum given in a modified experimental arrangement. Not only at the beginning of the treatment but also every 6 h an infusion of 200,000 KIE Trasylol was given during the period of the acute alcohol withdrawal syndromes. Time as well as intensity of symptoms (quantitatively measured by needed chlormethiazol) did not differ significantly between the aprotininum and the placebo group. 7 references. (Author abstract modified)

215738 Wyler, Allen R.; Wilkus, Robert J.; Troupin, Allan S. Department of Neurological Surgery, University of Washington, Mail Stop RI-20, Seattle, WA 98195 **Methysergide in the treatment of narcolepsy.** Archives of Neurology. 32(4):265-268, 1975.

Five patients with narcolepsy (four with the allied symptom of cataplexy) were treated with the serotonin antagonist methysergide. All patients had as good control of their sleep attacks while on methysergide therapy as on a control period of dextroamphetamine therapy. The cataplexy was less well controlled by methysergide than by dextroamphetamine, but improved when compared to a period without medication. Two patients developed severe calf claudication while on methysergide. 22 references. (Author abstract)

215858 Postma, J. U.; Tilburg, W. Van. Valeriuskliniek, Valeriusplein 9, Amsterdam-Zuid, Holland **Visual hallucinations and delirium during treatment with amantadine (Symmetrel).** Journal of the American Geriatrics Society. 23(5):212-215, 1975.

In 13 elderly patients, 12 of whom had Parkinson's disease, visual hallucinations and delirium developed as a side-effect of amantadine hydrochloride (Symmetrel) therapy. The symptoms promptly disappeared when amantadine was discontinued. Thereafter, each parkinsonian patient was treated satisfactorily with levo-dopa. Treatment with a combination of amantadine and an anticholinergic agent increases the likelihood of delirium because of the hazard of retention of urine. Although amantadine is effective in the treatment of Parkinson's disease in the elderly, the incidence of delirium as a complication seems higher in this age group. 17 references. (Author abstract)

216183 Horowitz, Harvey A. Adolescent Treatment Unit, Institute of the Pennsylvania Hospital, 111 North 49th St., Philadelphia, PA 19139 **The use of lithium in the treatment of the drug-induced psychotic reaction.** Diseases of the Nervous System. 36(4):159-163, 1975.

The use of lithium in the treatment of the drug induced psychotic reaction is discussed. It is suggested that a syndrome exists, characterized by a disturbance of affect, motility, and thinking which is precipitated by lysergic acid diethylamide (LSD). It is further suggested that there exists within the group of patients who have a psychotic reaction to LSD ingestion, a subgroup of individuals who are predisposed to a primary affective disorder, and who will express a LSD reaction in a manic form. Research findings are presented to demonstrate that this group is likely to respond to treatment with lithium. 30 references.

216339 Livingston, Samuel; Berman, Wulfred. Johns Hopkins University School of Medicine, Baltimore, MD **Comprehensive management of epilepsy.** Current Psychiatric Therapies. 14:175-188, 1974.

General treatment in cases of epilepsy is discussed, with emphasis placed on diagnosis and a comprehensive medical history, including age at onset, and prodromal features of the symptomatology. Also provided are the general principles of antiepileptic drug therapy, including physician visits at regular intervals, selection of appropriate drugs, combined therapy for the treatment of petit mal, use of single drugs, daily medication, dosage, period of drug intake, and discontinuation of drugs. The management of side-effects of antiepileptic drugs is considered, including drowsiness, ataxia, hyperactivity, gingival hyperplasia, skin rashes, blood, liver and kidney diseases. Possibilities of surgical treatment are also noted. 14 references.

216390 Ogura, Chikara; Nakazawa, Kazuyoshi; Kishimoto, Akira; Okuma, Teruo. Department of Neuropsychiatry, Tottori University School of Medicine, Tottori, Japan **A case of narcolepsy improved by lithium carbonate.** Clinical Psychiatry (Tokyo). 17(1):59-63, 1975.

A case of narcolepsy improved by lithium carbonate is discussed. A 17-year-old highschool boy had narcolepsy which appeared about once a month and lasted for 5-7 days. He was treated with methylphenidate without improvement. Lithium carbonate, however, completely eliminated his symptoms, which reappeared whenever treatment with this drug was terminated. 16 references.

216464 Bouvier, J. B.; Passeran, O.; Cherpin, M. P. no address **Psychometric study of Praxilene.** Journal of International Medical Research (North Hampton). 2:59-65, 1974.

The effects Praxilene were investigated in patients showing signs of decreased intellectual capacities due to progressive ischemia caused by arteriosclerosis. The clinical trial was in the form of a double-blind study with psychometric tests and statistical analysis. The results confirm the effectiveness of Praxilene in improving intellectual performance. This is particularly apparent with the less severely affected patients.

216485 Logue, G.; Nestadt, A.; Neumann, Yvonne. no address **The effects of pyrithioxine on the behaviour and intellectual function of learning-disabled children.** South African Medical Journal (Cape Town). 48(54):2245-2246, 1974.

A double-blind trial with pyritihoxine (Encephabol) and a placebo was carried out with 45 pairs of learning disabled pupils, the pairs equated in terms of certain variables. Both trial and control groups improved in reading and mechanical arithmetic over the 15 week period of the trial. However, the improvement was greater in the trial group particularly in arithmetic. The action of Encephabol on the brain is outlined and the purpose, patients, methods, and results of the trial are discussed.

216764 Planche, R.; Planche, S. C.H.U., 63000 Clermont-Ferrand, France **/Sulpiride and drug addiction./** Sulpiride et toxicomanie. Encephale (Paris). 1(1):49-52, 1975.

At the Ninth Congress of the International College of Neuro-psychopharmacology, Paris, July 1974, a paper was presented in which research concerning the use of sulpiride in drug addiction was presented. The results of administering sulpiride to drug addicts are difficult to evaluate since none of the patients were hospitalized and there was no way of ascertaining the exact doses taken by the patients. The patients usually present polytoxicomania and use hashish, opium derivatives, amphetamines, and usually lysergic acid diethylamide. Two recent observations summarize the action of sul-

piride. An attack of acute depersonalization in a young girl was suppressed in 8 days by administration of 1g of sulpiride per day. There was no relapse. An old drug addict injected at least 1g of sulpiride whenever he wanted to detoxify. He experienced no "flash" but could obtain a "soft" withdrawal, without the effects of the withdrawal syndrome. Neither dependence nor serious side-effects were observed. (Author abstract modified)

216966 Fenichel, Gerald M. Dept. of Neurology, Vanderbilt Univ. School of Medicine, Nahsville, TN 37232 **Pros and cons of drug therapy in the management of the hyperactive child.** Clinical Proceedings. 31(3):49-51, 1975.

The role of the physician in the management of hyperactivity is discussed. Hyperactivity is defined and the subject of behavioral therapy is discussed. The following topics are examined: the child for whom hyperactivity is a problem; causes of hyperactivity; treatments; indications for drug therapy; principles for the use of psychotropic drugs; and the adverse effects of drug therapy.

217001 Linka, Z. Detskiy psikhiatricheskiy dispanser, Budapest, Hungary **/The use of sidnocarb in child psychiatry./** Opyt primeneniya sidnokarba v detskoy psikhiatrii. Zhurnal nevropatologii i psikhiatrii imeni S. S. Korsakova (Moskva). 75(2):278-280, 1975.

The therapeutic effectiveness of sidnocarb was investigated in 50 adolescents suffering from neuroses, nocturnal enuresis, encephalopathy, or mental retardation. Sidnocarb was administered in average doses, and duration of therapy varied with the illness. Careful records were kept of the patients' psychic and somatic conditions. Effectiveness was evaluated by psychiatric results; subject opinion of the patient, and opinions of the child's peers, parents and teachers. Sidnocarb positively affected the psychic state of all subjects, but it was particularly effective in treating neuroses and nocturnal enuresis. The utilization of sidnocarb in child psychiatry was concluded to be very advisable. (Journal abstract modified)

217193 Schulz, J. Humboldt-Universitat zu Berlin, DDR-104 Berlin, Schumannstr. 20-21, E. Germany **/Differential diagnosis and therapy of sleep disturbances./** Differentialdiagnose und Therapie von Schlafstorungen im Alter. Zeitschrift fur Alternsforschung (Dresden). 28(1):49-52, 1974.

Sleep is characterized, and essential causes of sleep disturbances are presented. The particular importance of cardiovascular disease and psychic reaction pattern in the aged are emphasized. Recommendations for drug therapy are given on the basis of critical evaluation. 14 references. (Journal abstract modified)

217452 Carruthers-Jones, D. I. University Department of Psychiatry, Royal Edinburgh Hospital, Morningside Park, Edinburgh EH10 5HF **Effect of mesoridazine administration and withdrawal on performance in an older age group.** International Pharmacopsychiatry (Basel). 10(2):94-99, 1975.

The effect of mesoridazine administration and withdrawal on performance in older age groups were examined. Seven subjects, aged 48-62 years, took a placebo capsule nightly for 3 weeks, mesoridazine 10mg for 3 weeks, and then placebo for 3 weeks. Mesoridazine is a short half-life phenothiazine useful as a hypnotic. Performance was assessed during three experimental sessions on each test day. In spite of subjective sleepiness 20 min after rising, psychomotor performance 1-3 h later was not impaired, except possibly manual dexterity after the first dose. Neither auditory vigilance, nor digit symbol substitution were affected noticeably by the drug at any time of day. Card sorting of varying degrees of complexity was unimpaired, though there was a suggestion that the drug might be associated with better performance on the most complex task. 11 references. (Author abstract)

217523 Fann, William E.; Sullivan, John L., III; Miller, Robert D.; McKenzie, Gerald M. Department of Psychiatry, Baylor College of Medicine, 1200 Moursund, Houston, TX 77025 **Deanol in tardive dyskinesia: a preliminary report.** Psychopharmacologia (Berlin). 42(2):135-137, 1975.

Deanol, a central nervous system (CNS) stimulant and putative precursor of choline, was given to 10 subjects with tardive dyskinesia (TD). All subjects showed relief of symptoms of TD, possibly through enhancing CNS cholinergic mechanisms. 6 references. (Author abstract)

218010 DiMascio, Alberto; Goldberg, Harold L. Tufts University School of Medicine, Boston, MA **Managing disturbed geriatric patients with chemotherapy.** Hospital Physician. 11(6):35-39, 43, 46-48, 1975.

Recommendations are given for chemotherapy to improve the mood (to reduce psychiatric symptomatology), improve the cerebral circulation (to reverse primary symptoms of senile dementia such as memory loss and confusion), and improve the central nervous system function (to reduce behavioral manifestations of senile dementia) in disturbed geriatric patients. Actions, side-effects, and special considerations for the treatment of geriatric patients with specific drugs are discussed. Psychiatric states are defined, broad guidelines are given for managing elderly patients who are socially, psychologically, and physiologically disoriented. 6 references.

218011 Mizuguchi, Ryutaro; Hara, Tsunekatsu; Tanaka, Takao; Ichinowatari, Naomichi. Seishin-Igaku Institute, Tokyo, Japan **Serum concentrations of phenobarbital and diphenylhydantoin (preliminary report).** Bulletin of the Seishin-Igaku Institute (Tokyo). No. 19:47-54, 1974.

The serum concentrations of phenobarbital (PB) and diphenylhydantoin (DPH) in 89 epileptic patients were measured by a modified Svensmark and Kristensen's spectrophotometric procedure. No correlation was found between the frequency of epileptic seizure and the blood level of these drugs in a patient. The incidence of side-effects was, however, well correlated with the serum concentration of the drugs, and the toxic level of PB was estimated at 30microg/ml and of DPH at 15microg/ml. The serum level of PB was examined during the internal use of primidone. The results show the effective dose of primidone is equivalent to five times that of PB, and the daily dose of primidone should not exceed 16.6mg/kg to avoid its side-effects. 29 references. (Journal abstract modified)

218216 Kaplitz, Sherman E. Department of Neurology and Psychiatry, Oak Forest Hospital, 15900 South Cicero Ave., Oak Forest, IL 60452 **Withdrawn, apathetic geriatric patients responsive to methylphenidate.** Journal of the American Geriatrics Society. 23(6):271-276, 1975.

The effects of methylphenidate on withdrawn geriatric patients were assessed in a double-blind randomized study. It was found that, compared to placebo, methylphenidate was singularly effective in 44 withdrawn, apathetic geriatric patients. Patients receiving methylphenidate in a dosage of 20mg daily improved significantly over a period of 6 weeks as measured by results of tests for mental status, ward behavior

(nurses' rating), target symptom response, and physician's and nurses' global evaluations. For this reason and because there were no side-effects, this form of antidepressant therapy should be considered in the treatment of previously unresponsive or oversedated patients. 12 references. (Author abstract)

218217 Shader, Richard I.; Harmatz, Jerold S.; Kochansky, Gerald E.; Cole, Jonathan O. Massachusetts Mental Health Center, 74 Fenwood Road, Boston, MA 02115 **Psychopharmacologic investigations in healthy elderly volunteers: effects of pipradrol - vitamin (Alertonic) elixir and placebo in relation to research design.** Journal of the American Geriatrics Society. 23(6):277-279, 1975.

Ninety nine healthy elderly volunteers were tested to assess the effects of: 1) a pipradrol - vitamin (Alertonic) elixir, 2) a placebo, and 3) no treatment, during a 1 week period. The assessment measures were the Minnesota Multiphasic Personality Inventory Depression Scale, the Zung Depression Scale, Profile of Mood States, and the Wechsler Adult Intelligence Scale Digit Span. Alertonic had no significant effects on mood, memory or appetite, and the placebo effect was rarely greater than 50%. There were no significant side-effects. The findings demonstrate a valid method for studying psychotropic agents in the elderly. 6 references (Author abstract)

218306 Rosen, Herbert J. Doctors Building, 77 Union Street, Dover, NJ 07801 **Mental decline in the elderly: pharmacotherapy (ergot alkaloids versus papaverine).** Journal of the American Geriatrics Society. 23(4):169-174, 1975.

The effectiveness of dihydrogenated ergot alkaloids (DEA, Hydergine) versus papaverine in the treatment of selected symptoms associated with mental aging was evaluated. In a double-blind study, the effects of drugs were compared in relatively young geriatric patients, (mean age 65). After 12 wks of treatment, ratings of overall clinical condition and global change showed that the 26 patients given DEA had improved more than twice as much as the 27 patients given papaverine. Of the 14 individual symptoms rated, 13 improved significantly more in the DEA group, including confusion, dizziness, unsociability, depressive mood, and mental alertness. Other data confirmed the generally superior results with DEA. In view of its demonstrated beneficial clinical actions and of its notable scarcity of contraindications or side-effects, it is concluded that DEA is a significant pharmacologic contribution to the care of elderly persons showing selected symptoms of mental and functional decline. 14 references. (Author abstract modified)

218553 Eastham, R. D.; Jancar, J.; Cameron, J. D. Frenchay Hospital, Bristol, BS16 1LE, England **Red cell folate and macrocytosis during long-term anticonvulsant therapy in non-anaemic mentally retarded epileptics.** British Journal of Psychiatry (London). 126:263-265, 1975.

The occurrence of mild macrocytosis during long-term anticonvulsant therapy in nonanemic patients is discussed. Fifty nonanemic adult mentally retarded patients and 54 nonanemic adult mentally retarded epileptics treated with long-term anticonvulsants were given two yeast tablets, three times a day for 3 months. Results show that folate deficiency during long-term therapy can be simply and cheaply prevented by regular yeast supplement. 6 references. (Author abstract modified)

218564 Chartier, J.-P. Centre de sante d'hygiene mentale infanto-juvenile, 236, cours Lafayette, F 69003 Lyon, France /**Sulpiride and hyperkinetic syndromes.**/ Sulpiride et syndromes hyperkinetiques. Revue de Neuropsychiatrie Infantile etc. (Paris). 22(10-11):701-707, 1974.

The use of sulpiride in treating hyperkinetic syndromes is discussed. It is concluded, based on clinical observations, that sulpiride is a positive element in treating hyperkinetic children, but that it is only one element in the treatment of these children. Treating the parents is essential in conquering the children's avoidance mechanisms, which seem to be a defensive system against anxiety. Sulpiride is well tolerated, and when it is effective, it represents a means of attacking the root of the child's difficulties rather than merely the symptom. The failures in using this drug correspond to cases where treatment of the parents was not effective. 15 references.

219662 Dimitrova, P. Pleven, Bulgaria /**A comparative study of the effectiveness of enerbol and glutamic acid in oligophrenic children.**/ Sravnitelno izuchavane efektivnostta na enerbola s glutaminova kiselina pri oligofrenni detsa. Nevrologiya, psikhiatriya i nevrokhirurgiya (Sofia). 14(1):73-74, 1975.

The effectiveness of enerbol and glutamic acid in treating oligophrenia was investigated in children with restricted forms of oligophrenia and retarded mental development. Enerbol was found to be more effective than glutamic acid in treating the oligophrenic children. 5 references.

220271 Fuster, Pila; Tomas, Isabel; Cano Rosa. Facultad de Medicine, Universidad de Santiago de Compostela, Santiago de Compostela, Spain /**Psychopharmacology in child psychiatry: literature analysis.**/ Psicofarmacos en psiquiatria infantil: analisis bibliografico. Neurologia, Psiquiatria y Ciencias Afines (Madrid). 2(4):249-268, 1974.

Medical literature written on child psychopharmacology is analyzed by topic and diagnostic group. Statistics on the number of adult and child psychopharmaceutical books published and the most commonly used subdivisions of such works are provided. It is concluded that the use of certain nosological and diagnostic categories was apparently related to the nationality of the various authors. 17 references. (Journal abstract modified)

220284 Xhenseval, B. no address /**Deterioration syndromes in the elderly.**/ Syndromes de glissement chez les vieillards. Feuillets Psychiatriques de Liege (Liege). 7(1):26-34, 1974.

Deterioration syndromes in the elderly were investigated in a population of 88 patients aged over 65. Treatment included i.v. administration of 200-400mg/day of sulpiride, and neobehavioristic institutional therapy. In half the cases, a rapid evolution (24-48 hours) was observed with renewal of interest, object reinvestment and reduction in sulking and opposition. Kinesitherapy is recommended to preserve muscle tone in bedridden patients including rising from a chair, dressing, eating, and sphincter rehabilitation. Thymoanaleptic drugs of the monoaminoxidase inhibitor type are suggested for treating negative and manic-depressive states. For the senile patient, therapy becomes a substitute for social contact. 6 references.

220420 Panchenko, P. M. Leningradskiy nauchno-issledovatel'skiy psikhonevrologicheskiy institut im. V. M. Bekhtereva, Leningrad /**An aspect of biological therapy in the system of rehabilitationg epileptic patients with mental disorders.**/ Ob odnom iz aspektov biologicheskoy terapii v sisteme reabilitatsii bol'nykh epilepsiyey s psikhicheskimi narusheniyami. In: Kabanov, M., IV Mezhdunar. Simpoz. po Reabilit. Psikhicheski Bol'nykh. Leningrad, Psikhonevrologicheskiy Institut, 1974. 331 p. (p. 192-194).

In a paper presented at the Fourth International Symposium on Rehabilitation of the Mentally Ill held in Leningrad, Oc-

tober 1974, results of psychopharmacological treatment of 44 epileptic patients with disturbed blood brain circulation were reported. The prolonged administration of antiepileptic drugs had no effect; however, intracarotid novocaine injections significantly eliminated seizures and reduced the severity of mental disorder. (Journal abstract modified)

220829 Gehlen, W.; Eisenlohr, J. J. Universitats-Nervenklinik, D-5300 Bonn-Venusberg, Annaberger Weg, Germany **/Quantitative measurement of Parkinson disease rigor. Myointegrative drug trial in combination with the decarboxylase inhibiting drug Ro 8-0576./** Quantitative Rigormessung bei Morbus Parkinson: Myointegration zur Therapiekontrolle von L-Dopa in Kombination mit einem Decarboxylasehemmer (Ro 8-0576). Nervenarzt (Berlin). 45(1):22-29, 1974.

The effect on Parksinon's disease of L-Dopa therapy, in combination with the decarboxylase inhibiting drug Ro 8-0576/7 was measured. Eleven patients were subjected to 44 trials. In all patients symptoms decreased significantly after treatment, on the average by 62.7%. Degree of improvement depended on the extent of the disease prior to treatment, and on duration of treatment. Particular improvement was found in serious cases. The highest level of improvement was reached after 4-6 months. The relevance of the results for stereotactice surgery is discussed. 146 references. (Author abstract modified)

221103 Weber, Bruce A.; Sulzbacher, Stephen I. Child Development and Mental Retardation Center, University of Washington, Seattle, WA 98195 **Use of CNS stimulant medication in averaged electroencephalic audiometry with children with MBD.** Journal of Learning Disabilities. 8(5):300-303, 1975.

In a study undertaken to examine the effects of central nervous system (CNS) stimulants on averaged electroencephalic audiometry (AEA) thresholds, AEA was conducted on 12 children diagnosed as having minimal brain dysfunction (MBD). Each child was tested on three separate days to permit a double-blind evaluation of responsiveness to no drug, placebo and CNS stimulant drug conditions. Nine of the children were tested a fourth time to examine two dosage levels. Lower thresholds were recorded when the subjects were tested on medication. This suggests that AEA with MBD children can be enhanced by medication prescribed to counteract hyperactivity. The AEA performance of children on whom medication had a favorable effect was different from that of poor drug responders, even in the no medication conditions. 5 references. (Author abstract modified)

221289 Rosenberg, L. Psychiatrische Klinik II der Freien Universitat Berlin, 1 Berlin 19, Nussbaumallee 36 **/Double-blind test of three antidepressants, fourth communication; results with the Hamburg Depression Scale./** Doppelblindprufung von drei Antidepressiva, 4. Mitteilung: Ergebnisse mit der Hamburger Depressions-Skala. Arzneimittel-Forschung (Aulendorf). 24(2):207-213, 1974.

The effects of noxiptiline, nornoxiptiline and amitriptyline on a mixed diagnostic group of 149 patients were assessed via the Hamburg Depression Scale. Item based analysis indicates a better antidepressant effect with nornoxiptiline. No difference was found between drugs in an analysis of variance between scales. Sex related differences in drug effects were not discerned. It is concluded that no substantial differences exist between the three drugs. Methodological problems encountered in the experiment are discussed. 6 references. (Journal abstract modified)

221352 no author. no address **More evidence favors youth drug: first double-blind trials show Gerovital has some effect on aging.** Medical World News. 16(15):64, 1975.

Two double-blind clinical trials of the procaine based Romanian "youth drug", Gerovital HG, are reported. Studies by William W. K. Zung and H. S. Wang, both at the Duke University aging studies center, indicate that the drug does have some effect on the pathophysiology of aging. Using five measures of depression and anxiety, it was found that Gerovital compares Favorably with imipramine in alleviating depression, while physiological measures revealed that Gerovital may be have fewer side-effects than imipramine in elderly patient groups. Progress in other research projects using Gerovital is discussed.

221518 Franzen, Goran; Lenninger, Sven; Stigmar, Inger. University of Lund, Institute of Psychiatry, St. Lars Hospital, S-220 06 Lund, Sweden **Clinical Evaluation of Metylperone (Buronil) with epileptics.** Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(1):23-28, 1974.

Metylperone, a neuroleptic of butyrophenone type with a presumed anticonvulsive effect was tested in 11 institutionalized epileptics. No statistically significant differences in frequency of seizures (grand mal attacks and absences) or psychiatric rating (Nurses Observation Scale for Inpatient Evaluation NOSIE-30 compared to a control group consisting of 13 similar patients treated with conventional neuroleptics were observed. Sedative effects reported earlier in the literature were not observed, but rather a certain tendency toward increased activity. It is concluded that metylperone in selected cases is a good therapeutic alternative in the treatment of mental disturbances in epileptic patients. 17 references. (Author abstract modified)

221537 Turunen, Sakari; Larmo-Mattinen, Anneli. Paimio centralanstalt, SF-21520 Naskarla, Finland **/Clozapine as a sedative./** Klozapin som sedativum for utvecklingsstorda. Nordisk Psychiatrisk Tidsskrift (Hisings Backa). 29(2):103-107, 1975.

Clozapine and chlorpromazine were compared for their sedative efficacy in a double-blind trial of 8 weeks duration, in which 40 institutionalized mentally retarded patients aged 15 to 50 participated. Both preparations were found effective and neither of them could be statistically proven superior. 5 references. (Author abstract)

221561 Andersson, Poul Gertz. Hans Brogesvej 3 B, DK-8220 Brabrand, Denmark **/Amitriptyline treatment of patients with migraine./** Amitriptylin-behandling af patienter med migraene. Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(4):227-230, 1974.

The effect of treatment with amitriptyline in patients suffering from migraine is investigated. Twenty six patients (22 females and 4 males) suffering from attacks of common and classic migraine were treated for an average 2.6months with 30-75mg amitriptyline tablets. Attack frequency was reduced by 43%. The migraine index was reduced by 51%. Excepting weight gain, side-effects were not discouraging. A double-blind trial with cross-over technique is suggested to compare amitriptyline with other prophylactic drugs. 8 references. (Author abstract modified)

221639 Harnryd, Christer; Bjerkenstedt, Lars; Lindholm, Halvar; Ljungberg, Lennart. Beckomberga sjukhus, Fack, S-161 04 Bromma 4, Sweden **/A controlled clinical experiment**

with Buronil and haloperidol in disorientation among elderly patients./ En kontrollerad klinisk provning av Buronil och haloperidol vid forvirringstillstand hos aldre patienter. Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(6):469-472, 1974.

Buronil (methylperone) and Haldol (haloperidol) were tested in 44 women over 65 with senile agitation and confusion in a double-blind experiment lasting 2 weeks. No significant difference was found in the frequency of side-effects. In the methylperone group, changes in intensity of agitation, fussiness, and sleep requirements were statistically significant. In the haloperidol group no significant improvement was observed for some symptoms. Differences between the two preparations were not significant beyond the .05 level. 8 references.

221671 Rainaut, J. Centre Psychiatrique, 13-Aix-en-Provence, France **/A statistical analysis of the comparative double-blind study of the activity of loxapine and thioridazine./** Analyse statistique de l'etude comparative double insu de l'activite de la loxapine et de la thioridazine. Encephale (Paris). 1(2):147-160, 1975.

At the 9th International Congress of Neuropsychopharmacology, held in Paris, in July 1974, a paper was presented in which the results of a double-blind study comparing loxapine and thioridazine were reported. Fifty patients -- 37 schizophrenics and 13 chronic, nonschizophrenic psychotics -- received either 10mg loxapine or 50mg thioridazine for 12 weeks. With the 36 schizophrenics, loxapine and thioridazine reduced the patients' symptoms. With the 13 psychotics, the long-term activity of loxapine was at least as significant as that of thioridazine. Several items and factors on the Brief Psychiatric Rating Scale and the Nurses' Observation Scale for Inpatient Evaluation show a slightly more favorable result in the group treated with loxapine. These items were disorientation, disorder of thinking and excitation - disorientation. 11 references.

221885 Deze, J. Elena-Klinik, 35 Kassel-Harleshausen, Klinikstr. 5-16, Germany **/New prospects of treatment of Parkinson's disease with "ParKS-Plus"./** Neue Moglichkeiten in der Behandlung des Parkinson-Syndroms mit ParKS-Plus. Medizinische Welt (Stuttgart). 25(15):663-667, 1974.

A pilot study testing the therapeutic effectiveness of the new drug "ParKS-Plus" in 100 patients with Parkinson's disease is reported. ParKS-Plus is a combination of the anticholinergic "ParKS 12" with the antidepressant substance amitriptyline. Alleviation of depressive moods is held to be an important factor for therapeutical success. Fifty nine patients (20 women, average duration of disease 5 years) were treated with ParKS-Plus only, in controlled treatment lasting 6-8 weeks. Effect on rigor was high in 36, and very high in 15 cases. Tables on age, sex, and pathogenesis (broken down into endogenic, postencephalitic, vascular, and uncertain genesis) and on specificity of effect are given. Best results were found with vascular genesis. Medical histories of four patients are given in detail. A second group of 41 patients (15 women) was treated with a combination of ParKS-Plus and L-dopa. The same tables are given. Results were similarly good, and positive particularly on depressive moods. 22 references.

221934 Ballard, Joyce Elaine. University of Illinois, Urbana-Champaign **The effects of methylphenidate during rest, exercise, and recovery upon the circulorespiratory responses of hyperactive children. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-14079 HC$13.50 MF$5.00 240 p.

To evaluate the effect of methylphenidate on the circulorespiratory responses of hyperactive children under the conditions of rest, exercise stress, and recovery from exercise stress, 27 hyperactive children (7 to 13 years old) received the medication. Results show that: 1) methylphenidate produced significantly increased heartrate and blood pressure responses throughout rest, exercise and recovery; 2) at dosage levels of 0.55mg/kg and higher, it produced blood pressure responses at a hypertensive level; 3) tolerance to methylphenidate medication did not develop for the circulorespiratory responses measured during rest, exercise and recovery; 4) methylphenidate produced slight changes in the per minute oxygen intake recorded during exercise and recovery, but significant alteration of the total cost of the standardized exercise was not found; and 5) circulorespiratory responses obtained for the hyperactive children on their placebo tests were significantly higher during rest and exercise than were the responses of controls to the same testing conditions. (Journal abstract modified)

222747 Prichep, Leslie S. City University of New York **Attention and the auditory evoked potential in hyperkinetic children treated with methylphenidate and in normal children. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-12689 HC$13.50 MF$5.00 186 p.

Differences between hyperkinetic children and nonhyperkinetic normal children and the effects of methylphenidate on hyperkinetic children, were investigated under conditions of differential attentional demands. Auditory average evoked potentials were recorded from vertex under conditions of certainty and uncertainty. In the certain condition the subject was told prior to each trial whether he would hear a single or double click. In the uncertain condition the subject was required to predict whether the next trial would consist of a single or double click. In the uncertain condition the subject was required to predict whether the next trial would consist of a single or a double click and received a monetary reward for correct guesses. The interval in the double click was 950 milliseconds. Differences between the groups were largest in response to the second click under conditions of uncertainty, where attentional demands were maximal. Under these conditions, the late components in the response of the nonhyperkinetic normal children were more positive than those of the hyperkinetic children. (Journal abstract modified)

224086 Iovlev, B. V.; Kozlov, V. P.; Kharitonov, R. A. Leningradskogo nauchno-issledovatel'skogo psikhonevrologicheskogo instituta im. Bekhtereva, Leningrad **/Prognosis of the therapeutic effect of suxilep and trimetin using a successional statistical procedure./** Prognozirovaniye terapevticheskogo effekta suksilepa i trimetina s pomoshch'yu psoledovatel'noy staticheskoy protsedury. Zhurnal nevropatologii i psikhiatrii imeni S. S. Korsakova (Moskva). 75(5):748-752, 1975.

The use of computer diagnostics in predicting the disappearance of seizures was investigated during treatment of minor forms of epilepsy in 176 children and adolescents with trimetin and suxilep. A special prognostic table was made, based on a successional statistical procedure. One hundred nineteen patients were treated with trimetin; 57 were treated with suxilep. Comparison with a control group showed computer diagnostics to be effective in predicting the outcome of suxilep therapy (correct predictions were made in 80% of the cases), but far less accurate in predicting the therapeutic effect of trimetin (accurate prognoses were made in one third of the cases). 15 references. (Journal abstract modified)

224392 Sato, Keiichi; Kaneko, Sadao. Jinkeikai Sato Hospital, Japan **Trial experience of neoproserin in the psychiatric area.** Medical Consultation & New Remedies (Tokyo). 11(10):2189-2199, 1974.

The effect of neoproserin on various types of mental illness was studied, based on an experiment in which 40 mental patients with depression, schizophrenia, psychogenic reaction, epilepsy and other disturbances were treated intramuscularly for 1-19 months. This drug was effective in 85% of the patients. Weight gain was observed, but no other side-effects were noted. 5 references.

224394 Naganuma, Rokuichi; Yamamoto, Katsumi; Inanaga, Kazutoyo. Department of Neuro-psychiatry, Kurume University School of Medicine, Kurume, Japan **Experience of using Lorazepam, a new tranquilizer.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(11):1225-1236, 1974.

The effect of lorazepam on various psychiatric symptoms was studied, based on an experiment in which 88 patients with neurosis, borderline psychosis, schizophrenia and depression were treated from 1 week to 1 year 10 months. The drug proved effective in the majority of patients. It was especially effective in those suffering from neurosis. Side-effects such as drowziness and dizziness were observed in some cases. 8 references.

224395 Ohara, Kenjiro; Ikeda, Hiroshi; Maruyama, Shin; Komatsu Junichi. Department of Neuro-psychiatry, Jikei University School of Medicine, Tokyo **Experience of using Lorazepam (WY 4036) in psychiatry.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(11):1237-1244, 1974.

The effect of lorazepam on anxiety, irritation and depression was studied, based on an experiment in which 34 patients with depression, neurosis, psychosomatic diseases, psychogenic reaction, arteriosclerosis, schizophrenia, epilepsy and tic were treated orally for 14-127 days with or without other psychotropic drugs. The rate of effectiveness was 88.2%. Side-effects was observed in 20.6%, but they were minor and did not require termination of treatment. 88 references.

224584 Freche, Ch. Hopital Foch, 40, rue Worth, 92151 Suresnes, France **/Study of an anxiolytic drug, clobazam, in O.R.L. with pharyngeal psychosomatic manifestations./** Etude d'un anxiolytique clobazam en O.R.L. dans les manifestations psychosomatiques pharyngees. Semaine des Hopitaux Therapeutique (Paris). 51(4):261-263, 1975.

The anxiolytic drug, clobazam, was administered to 40 patients presenting with pharyngeal psychosomatic manifestations, including hiatus hernias, chronic pharyngitis, and pharyngeal paresthesias. The drug had good results in 18 out of 20 cases (90%). It was less effective in treating true pharyngitis, presenting favorable results in five cases out of six. It was very effective in treating pharyngeal paresthesias, with excellent results in six cases, favorable results in six cases, and moderate results in two cases, of a total 14 cases treated. A moderate dose ensured effective treatment without inducing behavioral changes in the subjects. Tolerance was perfect, and there were no side-effects.

224585 Theodorides, M. no address **/Sulpiride trial in child psychiatry./** Essai du sulpiride en pedopsychiatrie. Semaine des Hopitaux Therapeutique (Paris). 51(4):281-282, 2975.

Sulpiride was administered to a population of children suffering from behavioral disturbances, enuresis, and mental retardation. With behavioral disturbances and retardation, the overall results were very good, with 17 cases of success and three failures. The three failures were in prepsychotic states. With enuresis, there were three cases of favorable results out of seven. The thymoanaleptic characteristics, execellent neurovegetative tolerance, and disinhibiting effect of sulpiride are noted. Tolerance was excellent, and it did not cause sleep disturbances or extrapyramidal symptoms.

224855 Gittelman-Klein, Rachel; Klein, Donald F. Queens College, Flushing, New York 11367 **Ritalin versus behavior therapy in hyperactive children.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 193-194).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, a paper was presented which reported results of a two year ongoing study of the relative efficacy of methylphenidate (Ritalin) and behavior therapy in hyperkinetic children. Ss between 6 and 12 years of age were assigned to one of three treatments: methylphenidate; behavior therapy and placebo; behavior therapy and methylphenidate. Results indicate that all three treatments produced improvement, with the most marked improvement in the combination group of behavior therapy and methylphenidate. In the behavior therapy group, of all raters, parents perceived the most improvement, while psychiatrists were less impressed. Classroom observations indicate that behavior therapy was effective over an eight week period, but a marked tendency for relapse occurred over the following four weeks. Results indicate that behavior therapy can be used at least temporarily for amelioration of distractible, inappropriate, disruptive behavior of hyperkinetic children. Its therapeutic impact is not as marked as that of methylphenidate, and undertaking such a program is extremely costly. (Journal abstract modified)

224910 Bruun, Ruth Dowling; Shapiro, Arthur K.; Sweet, Richard D.; Shapiro, Elaine; Solomon, Gaile; Wayne, Henrietta L. Department of Psychiatry, New York Hospital, Cornell Medical Center, New York, NY **A follow-up of Tourette's syndrome in seventy-seven patients.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 257-258).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, May 1975, a paper was presented reporting the course of Tourette's Syndrome after chemotherapy using haloperidol between 1964 and 1973. All but one patient taking haloperidol reported some improvement, with patients originally rated as either mild or severe showing less improvement than those originally rated as moderate to marked. Improvement significantly increased with increasing length of treatment time. Patients on haloperidol and another medication showed an average improvement of 74.7%; all patients on haloperiodol alone, however, were dissatisfied. EEG and neurological abnormalities, organicity on psychological testing, and age of onset had no significant relationship to response. Adolescence to young adulthood was unquestionably the period of greatest instability. (Journal abstract modified)

225281 Papaspiropoulos, S. Beckomberga sjukhus, 161 04 Bromma 4, Sweden **/Clinical trial with flupentixol (Fluanxol) in the treatment of denile dementia./** Klinisk provning av flupentixol (Fluanxol) vid behandling av senil demens. Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(8):597-603, 1975.

Flupentixol (Fluanxol) was administered to 40 elderly female patients suffering from senile dementia. In the three week ex-

periment, effects and side-effects were recorded. A rating scale of 16 symptoms was used jointly by doctors, nurses, and social workers. The dosage of 1mg daily was constant in all patients after the third day. Of the 40 patients, 82% showed improvement, especially in reduced confusion, aggressiveness, irritability, and agitation, as well as in increased activity. Except for a few cases of sleep disturbances, flupentixol was almost free from side-effects in the doses used. 7 references. (Author abstract modified)

12 PSYCHOTOMIMETIC EVALUATION STUDIES

213702 Albaugh, Bernard J.; Anderson, Philip O. Department of Social Services, U. S. Public Health Service Indian Hospital, Clinton, OK 73601 **Peyote in the treatment of alcoholism among American Indians.** American Journal of Psychiatry. 131(11):1247-1250, 1974.

The development and effectiveness of a treatment program for alcoholism among American-Indians was studied. This program offers the alcoholic Indian both occupational and cultural therapy, including participation in the services of the Native American Church (peyote meetings). During these meetings, participants often ingest peyote (mescaline), which, like lysergic acid diethylamide, facilitates cathartic expression and enhances suggestibility. 20 references. (Journal abstract modified)

216999 Anokhina, I. P.; Bondarenko, T. T.; Zabrodin, G. D.; Khristolyubova, N. A. Laboratoriya psikhfarmakologii, Tsentral'nogo nauchno-issledovatel'skogo instituta sudebnoy psikhiatrii im. prof. Serbskogo, U.S.S.R. **/Some general principles of the mechanism of the central action of psychotomimetics./** Nekotoryye obshchiye printsipy mekhanizma tsentral'nogo deystviya psikhotomimetikov. Zhurnal nevropatologii i psikhiatrii imeni S. S. Korsakova (Moskva). 75(2):264-274, 1975.

The neurophysiological and neurochemical effects of lysergic acid diethylamide (LSD), amphetamines and hashish extract on the central nervous system were investigated in rabbits and mice. Neurophysiological studies with the introduction of electrodes into various parts of the brain showed that all the psychotomimetics elicited activation of cerebral biological currents, particularly in the midbrain reticular formation and in parts of the limbic system. Biochemical studies showed that all the psychotomimetics affected the metabolism of noradrenaline and serotonin concentration in the brain: the noradrenaline level decreased in the midbrain and hypothalamus; changes in serotonin content were inconsistent. Histochemical studies showed that the psychotomimetics manifested expressed chemical action selectivity. When the effects of psychotomimetics were compared with those of parabromoamphetamine, a preparation lacking psychotomimetic properties, psychomimetic effects were found to be nonspecific. 13 references. (Journal abstract modified)

217557 Shulgin, Alexander T.; Carter, Michael F. 1483 Shulgin Road, Lafayette, CA 94549 **Centrally active phenethylamines.** Psychopharmacology Communications. 1(1):93-98, 1975.

The two carbon homologs of two potent psychotomimetic agents are described. Unlike the parent isopropylamine compounds (4-methyl-2,5-dimethoxyamphetamine (DOM, STP) and 4-bromo-2,5-dimethyoxyamphetamine (PBR, 4-BR)) these phenethylamines lead to an intoxication state which is, in normal subjects, of short duration and of greatly increased sensory enhancement, but which does not superimpose hallucinogenesis. These two phenethylamines, 4-methyl-2,5-dimethoxyphenethylamine and 4-bromo-2,5-dimethoxyphenethylamine are active in man at oral levels of 0.1to 0.2mg/kg, approximately 1/10 the potency of their three carbon counterparts. 9 references. (Author abstract)

217821 Hirschhorn, I. D.; Hayes, R. L.; Rosecrans, J. A. Department of Pharmacology, Medical College of Virginia, Richmond, VA **Discriminative control of behavior by electrical stimulation of the dorsal raphe nucleus: generalization to lysergic acid diethylamide (LSD).** Brain Research (Amsterdam). 86(1):134-138, 1975.

In a study of discriminative control of behavior by electrical stimulation of the dorsal raphe nucleus of the rat, lysergic acid diethylamide (LSD), in sufficient doses, produced responding appropriate to electrical stimulation. There was only a moderate, and statistically insignificant, alteration in responding during the stimulation condition. A decrease in the rate of responding produced by 100 micro ug/kg of LSD precluded the testing of a higher dose of LSD. These results indicate that electrical stimulation of the dorsal raphe nucleus and LSD have similar stimulus properties. Another common behavioral effect of LSD and stimulation of serotonergic neurons is their impairment of habituation to repetitive sitmuli. These results are consistent with the hypothesis that LSD produces at least some of its perceptual effects by mimicking the action of 5-hydroxytryptamine in the brain. The results demonstrate that comparing the stimuli produced by electrical brain stimulation of certain brain areas with the stimulus properties of drugs is a viable technique. 17 references.

219181 Marquis, William James. Michigan State University A **behavioral analysis of hallucinogenic drugs. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-7209 HC$13.50 MF$5.00 210 p.

The behavioral effects of hallucinogenic drugs, including DOM, lysergic acid diethylamide (LSD), psilocybin, and d-amphetamine, were studied in a series of experiments. Results indicate that operant conditioning paradigms can be a useful tool for characterizing hallucinogenic properties of psychoactive drugs, as well as for differentiating agents within the hallucinogenic drug class. Further, these schedules provided a practical means for assessing tolerance phenomena and cross-tolerance relationships between hallucinogenic drugs, since the results with rats as Ss correlated well with data derived from human studies. Finally, the use of these schedules for drug interaction experiments provided data that may well be useful for ascertaining the mechanisms of action of hallucinogenic drugs. Since these techniques yielded unique behavioral profiles for hallucinogens, they should prove useful in psychiatric research for testing endogenous compounds that are potentially instrumental in initiating naturally occurring psychoses. (Journal abstract modified)

221044 Smith, Robert C.; Boggan, William O.; Freedman, Daniel X. Department of Psychiatry, University of Chicago, 950 E. 59th St., Chicago, IL 60637 **Effects of single and multiple dose LSD on endogenous levels of brain tyrosine hydroxylase and catecholamines.** Psychopharmacologia (Berlin). 42(3):271-276, 1975.

The effects on brain catecholamines of seven daily doses of d-lysergic acid diethylamide (LSD) injected to Sprague-Dawley rats on a tolerance dosage schedule were compared with the effects of a single dose of LSD over a 90 min time course. Compared to saline controls, after a single dose of LSD, there was a significant decrease in brain norepinephrine at 30 and 60

min, a rise in dopamine at 60 min, and a small rise in brain tyrosine at early time points followed by significant decline from control levels after 60 min. The effects of a single dose of LSD were similar to the higher sequential doses but were greater in both magnitude and duration of the brain catecholamine changes. After a tolerance dosage schedule there were significant changes in the response of brain catecholamines to LSD. The rise in brain dopamine at 60 min was abolished, brain tyrosine was uniformly below both saline and single dose animals, and brain norepinephrine returned to control levels slightly faster. 37 references. (Author abstract modified)

223921 Naranjo, Claudio. no address **The healing journey: new approaches to consciousness.** New York, Pantheon Books, 1974. 235 p. $6.95.

Experiments with four drugs which are quite different from the better known stimulants, depressants, hallucinogens and psychedelics are described. Two of the drugs are called "feeling enhancers," and are derived from the essence of nutmeg; MDA provides egolessness, MMDA a clarity which is experienced as a peak experience. The second pair of drugs dealt with are called "fantasy enhancers": Harmaline, which aids patients in eliciting their significant symbols and archtypical experiences, and Ibogaine, which promotes the memory of inner events. A taxonomy of altered states of consciousness is presented, and it is shown how both the enhancement of pathology and peak experiences are strategies best understood as contrasting reality and illusion.

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOG

213703 Pauling, Linus. Linus Pauling Institute of Science and Medicine, 2700 Sand Hill Rd., Menlo Park, CA 94025 **On the orthomolecular environment of the mind: orthomolecular theory.** American Journal of Psychiatry. 131(11):1251-1257, 1974.

Orthomolecular psychiatry is discussed as the achievement and preservation of good mental health by the provision of the optimum molecular environment for the mind, especially the optimum concentrations of substances normally present in the human body, such as the vitamins. It is suggested that there is sound evidence for the theory that increased intake of such vitamins as ascorbic acid, niacin, pyridoxine, and cyanocobalamin is useful in treating schizophrenia. 35 references. (Journal abstract modified)

213705 Klein, Donald F. Department of Psychiatry, Long Island Jewish-Hillside Medical Center, P. O. Box 38, Glen Oaks, NY 11004 **/Comment on Linus Pauling's theory of orthomolecular psychiatry./** Comment. American Journal of Psychiatry. 131(11):1263-1265, 1974.

The use of megavitamin therapy in the treatment of a variety of psychiatric disorders proposed by Linus Pauling is discussed in terms of scientific inference and therapeutic ethics. The problems with the double-blind trial in drawing conclusions about the efficacy of vitamin C in the treatment of psychotics and schizophrenics are evaluated. The significance of a drug that affects 30% of the population tested is discussed in terms of statistical inference. The ethical principles involved in the long-term clinical care of a patient are considered. 4 references.

213782 Kragh-Sorensen, Per. Clinical Pharmacology Research Unit, Danish State Medical Research Council, Copenhagen, Denmark **The relationship between nortriptyline plasma levels and clinical effects.** Proceedings of the Royal Society of Medicine (London). 68(2):99-102, 1975.

At the February 12, 1974 meeting of the Royal Society of Medicine, a paper was presented which reported the relationship between nortriptyline (NT) plasma levels and clinical effects. The kinetic behavior of the drug was examined, and it was found that the plasma concentration is determined mostly by the rate of metabolism. Side-effects were associated with very high plasma levels, and they were correlated with plasma level, but not with dosage. A pilot study showed the optimal plasma level for therapeutic effectiveness, and a second study attempted to demonstrate a curvilinear relationship between plasma level and the effect of NT. The existence of an upper limit for the therapeutic concentration range was hypothesized. A complicated triple-blind study now in progress is described, and a followup study of 22 patients successfully treated with NT is also discussed. 15 references.

214011 Silverstone, T.; Schuyler, D. Psychiatric Unit, German Hospital, Dalston, E8, England **The effect of cyproheptadine on hunger, calorie intake and body weight in man.** Psychopharmacologia (Berlin). 40(4):335-340, 1975.

The appetite stimulating action and the weight gaining potential of 1 month's treatment with the antihistamine and antiserotonergic compound cyproheptadine (Periactin) 4mg three times daily was compared to placebo in a double-blind crossover trial in 16 thin but otherwise normal volunteers who wanted to gain weight. Subjects gained significantly more weight on cyproheptadine than on placebo. There was also a corresponding relative increase in subjective hunger ratings and food intake during the period on active drug. Drowsiness was the most frequent side-effect observed. These findings are discussed in relation to a possible serotonergic feeding mechanism. 17 references. (Author abstract)

214885 Maeda, Kiyoshi; Kato, Yuzuru; Ohgo, Shozo; Chihara, Kazuo; Yoshimoto, Yoshio; Yamaguchi, Naohiko; Kuromaru, Seishiro; Imura, Hiroo. Department of Neuropsychiatry, Kobe University School of Medicine, Kobe, Japan **Growth hormone and prolactin release after injection of thyrotropin-releasing hormone in patients with depression.** Journal of Clinical Endocrinology and Metabolism. 40(3):501-505, 1975.

The effects of thyrotropin-releasing hormone (TRH) on the release of growth hormone (GH), prolactin (PRL), and thyrotropin (TSH) were investigated in patients with depression. Intravenous injection of synthetic TRH caused a significant increase in plasma GH in eight of 13 patients with mental depression. After clinical recovery, these patients had no response of plasma GH to TRH. TRH administration did not raise plasma GH in normal Ss. Plasma PRL responses to TRH were significantly enhanced in depressed patients compared with control Ss. Plasma TSH responses to TRH were significantly blunted in patients with depression. These results suggest disorders in the hypothalamo-pituitary function in depression. 31 references. (Author abstract)

215014 Kantor, Shepard J.; Bigger, J. Thomas, Jr.; Glassman, Alexander H.; Macken, Daniel L.; Perel, James M. New York State Psychiatric Institute, 722 W. 168th St., New York, NY 10032 **Imipramine-induced heart block: a longitudinal case study.** Journal of the American Medical Association. 231(13):1364-1366, 1975.

The case of a 74-year-old man in whom a 2:1 heart block developed during a prospective study designed to evaluate the effects of therapeutic doses of imipramine hydrochloride on heart function is reported. Serial cardiographic studies and determinations of blood imipramine concentrations showed that the heart block was directly related to the plasma concentration of the drug and occurred below the atrioventricular node in the His-Purkinje system. 18 references. (Author abstract)

215064 Misurec, J.; Nahunek, K.; Svestka, J.; Rodova, A. Psychiatric Clinic Brno-Bohunice, Jihlavska 102, Czechoslovakia **EEG changes in the treatment with octoclothepine in very high doses.** Activitas Nervosa Superior (Praha). 16(4):244-245, 1974.

At the 16th Annual Psychopharmacological Meeting, Jesenik, 1974, a paper was presented which reported the influence on electroencephalograms of high doses of octoclothepine in 23 patients, aged 16 to 60, including 19 schizophrenics and four manic depressives. Therapy with very high doses was well tolerated by the majority of patients and led to improvement in some who were resistant to usual pharmacotherapy. The EEG changes on the 10th and 21st day of treatment were those of the EEG neuroleptic syndrome; all EEGs, except one borderline, were abnormal on the 21st day of treatment. In patients with a better clinical outcome, the EEG changes were more pronounced but the correlation did not reach the level of statistical significance. Occurrence of paroxysmal abnormalities, but not the intensity of slow activity, was related to the dosage. There was no relation between EEG changes and age when very high doses were given to all patients (doses 30-350 mg), and no correlation between EEG changes and the quantity and intensity of side-effects.

215070 Hynek, K.; Faber, J.; Tosovsky, J.; Cerny, M. Psychiatric Clinic, Ke Karlovu 11, 120 00 Prague 2 **The effect of combination of methylphenidate and diazepam on the EEG and its evaluation by means of discriminant analysis.** Activitas Nervosa Superior (Praha). 16(4):257-258, 1974.

At the 16th Annual Psychopharmacological Meeting, Jesenik, 1974, a paper was presented in which the effect of methylphenidate, diazepam, and their combination on the electroencephalogram (EEG) after a single application was evaluated quantitatively in 20 healthy students. Under the influence of the drugs and their combination, the alpha, theta, and delta activity decreased in frontal, central, and temporal regions significantly. Methylphenidate reduced beta activity while diazepam increased it. The effect of the combination was the same as after diazepam, but the increase was statistically significant only in left frontal, central, and temporal regions. Discriminant analysis shows that the mechanism of action of both drugs was different even in those frequency bands which, when evaluated with the t-test, yielded no significant differences.

215071 Faber, J.; Tosovsky, J.; Hynek, K. Neurological Clinic, Charles University, Prague **Factor analysis of EEG of healthy subjects given no drugs and a combination of diazepam and methylphenidate.** Activitas Nervosa Superior (Praha). 16(4):258-259, 1974.

At the 16th Annual Psychopharmacological Meeting, Jesenik, 1974, a paper was presented in which the effects of diazepam and methylphenidate on the electroencephalograms (EEG) of healthy Ss were described. An analysis of correlation coefficients of activity in the frontal, central, parietal, occipital, and temporal regions was included. Every frequency band behaved differently in the EEG after the drugs were administered. The absolute amount of a certain frequency above the skull areas and the correlations of this frequency between areas were two relatively independent phenomena. The number of factors was determined with the Lawly test, and were also interpreted by means of a correlation matrix. In the EEG of the tumor group as compared to a healthy group there occurred a certain simplification of the individual graph and interindividual uniformity.

215454 van Praag, H. M.; Dols, L. C. W.; Schut, T. Department of Biological Psychiatry, Psychiatric University Clinic, State University of Groningen, Groningen, The Netherlands **Biochemical versus psychopathological action profile of neuroleptics: a comparative study of chlorpromazine and oxypertine in acute psychotic disorders.** Comprehensive Psychiatry. 16(3):255-263, 1975.

Correlations between therapeutic effect and influence of neuroleptics on cerebral monoamine metabolism were studied. Chlorpromazine, a substance which reduces dopaminergic and noradrenergic transmission, was compared with oxypertine, a compound which chiefly reduces noradrenergic transmission. On the basis of biochemical considerations, three hypotheses were tested: 1) that chlorpromazine is superior to oxypertine as antipsychotic agent; 2) that the two substances are equivalent sedatives, but oxypertine is superior when loss of initiative is a prominent symptom; and 3) that oxypertine exerts less influence on extrapyramidal motor functions than chlorpromazine. Hypotheses 1 and 3 were confirmed; hypothesis 2 was partly confirmed. It is therefore recommended that oxypertine trials be started on a larger scale in psychoses associated with marked inertia. 27 references. (Author abstract modified)

215668 Lewis, James A.; Young, Rosemarie. EEG Laboratory, University of Colorado Medical Center, Denver, CO 80220 **Deanol and methylphenidate in minimal brain dysfunction.** Clinical Pharmacology and Therapeutics. 17(5):534-540, 1975.

Deanol, a putative acetylcholine precursor which has been used as a treatment for childhood hyperactivity was administered to children referred for problems with learning, including many with hyperactivity. Behavior rating forms, reaction time, and a series of standard psychometric tests were given before and after treatment. Both drugs showed significant improvement on a number of tests; the pattern and degree of change differed slightly for the two. In this paradigm, deanol thus appeared to improve performance in children with learning and behavior disorders. 52 references. (Author abstract modified)

215669 Bellville, J. Weldon; Swanson, George D.; Aqleh, Kamel A. Department of Anesthesiology, School of Medicine, University of California at Los Angeles, Los Angeles, CA 90024 **Respiratory effects of delta-9-tetrahydrocannabinol.** Clinical Pharmacology and Therapeutics. 17(5):541-548, 1975.

The respiratory effects of smoked marijuana and oral delta 9-tetrahydrocannabinol (THC) were studied in healthy males by assessing displacement of the respiratory response curve. Both cause slight respiratory depression. While alcohol usually causes respiratory depression, in some subjects it stimulates respiration. High doses of pentobarbital depress respiration but low doses apparently do not. 14 references. (Author abstract)

215671 Gram, Lars F.; Christiansen, Johannes. Department of Pharmacology, University of Copenhagen, 20, Juliane Maries Vej, DK-2100 Copenhagen, Denmark **First-pass metabolism of**

imipramine in man. Clinical Pharmacology and Therapeutics. 17(5):555-563, 1975.

The systemic availability of orally administered imipramine (IP) was examined in man. Availability varied from 29-77% in 4 subjects. The decrease in availability was due to an excess in metabolism after oral administration. This first pass metabolism did not correlated with plasma half-life, apparent clearance, or the rate of metabolite excretion in urine. There was close correlation with the excess in formation of demethylated metabolites after oral administration, which suggests that the first pass metabolism is mediated by demethylation, but does not correlate to the total rate of demthylation. 20 references. (Author abstract)

215672 Mandelli, M.; Morselli, P. L.; Nordio, S.; Pardi, G.; Principi, N.; Sereni, F.; Tognoni, G. Department of Child Health, Univeristy of Milan Medical School, Milan, Italy **Placental transfer of diazepam and its disposition in the newborn.** Clinical Pharmacology and Therapeutics. 17(5):564-572, 1975.

Diazepam (DZ) placental transfer in pregnant women at term, following single or repeated drug administration by various routes, was evaluated. DZ and its metabolite N-demethyldiazepam (NDZ) were constantly present in umbilical cord plasma at concentrations comparable to the mother's shortly after drug administration. N-methyloxazepam (MOX) was detected in cord plasma only in a limited number of cases following chronic DZ treatment. Postmortem analysis of fetal tissue concentrations showed accumulation of NDZ in heart and lungs. Differences in NDZ concentrations between venous cord (VC) and arterial cord (AC) plasma suggest metabolic degradation of DZ in the fetus. The DZ apparent plasma half-life in the newborn was found to be longer than previously observed in infants and children. The low drug clearance appears to be linked to reduced urinary excretion of hydroxylated metabolites, suggesting limited capability to dispose of DZ in the newborn. 35 references. (Author abstract)

215674 Shoulson, Ira; Chase, Thomas N. Laboratory of Neuropharmacology, National Institute of Neruological and Communicative Disorders and Stroke, Bethesda, MD **Fenfluramine in man: hypophagia assocaited with diminished serotonin turnover.** Clinical Pharmacology and Therapeutics. 17(5):616-621, 1975.

A double-blind trial of orally administered fenfluramine was conducted in 7 nonobese adults with various neurological disorders. Caloric intake and body weight fell significantly after 8 days of treatment although there was no definite change in appetite ratings. Average central turnover of serotonin, as estimated by the cerebrospinal fluid (CSF) accumulation of 5-hydroxyindoleacetic acid (5-HIAA) during probenecid loading, decreased by 66%. No significant change in homovanillic acid, the major dopamine product, was apparent. The results support the contention that the effect of fenfluramine on human dietary intake may be mediated by alterations in serotonergic rather than dopaminergic mechanism. 28 references. (Author abstract)

215697 Girke, W.; Krebs, F.-A.; Muller-Oerlinghausen, B. Psychiatric Department, The Free University of Berlin, Nussbaumallee 36, 1 Berlin 19, Germany **Effects of lithium on electromyographic recordings in man: studies in manic-depressive patients and normal volunteers.** International Pharmacopsychiatry (Basel). 10(1):24-36, 1975.

Seventeen female manic-depressive patients under long-term treatment with lithium salts were studied. Results showed a reduction of the maximal motor nerve conduction velocity (NCV) and of the duration of isolated potentials (IPs) in six cases. These changes, however, were not clearly due to the influence of lithium only. Psychopathology, additional medication, and other variables may have been also responsible for these findings. NCV and IPs as well as the concentration of electrolytes in serum and RBC were determined in seven healthy volunteers before, during, and after lithium administration. NCV was significantly decreased and the duration of IPs slightly increased after 1 week of lithium intake. The magnesium serum concentration increased steadily during the experimental period. Thus, the possibility cannot be excluded that symptoms of fatigue and muscular weakness in lithium treated patients might be caused at least partially by changes of the peripheral nervous muscular function. 44 references. (Author abstract)

215710 Sargent, T.; Kalbhen, D. A.; Shulgin, A. T.; Braun, Gisela; Stauffer, H.; Kusubov, Natalia. Donner Laboratory of Medical Physics and Biophysics, University of California, Berkeley, CA **In vivo human pharmacodynamics of the psychodysleptic 4-Br-2,5-dimethoxyphenylisopropylamine labelled with 82Br or 77Br.** Neuropharmacology (Oxford). 14(3):165-174, 1975.

The psychodysleptic compound 4-Br-2,5-dimethoxyphenylisopropylamine (4-Br-DPIA) was synthesized with 82Br or Br77 and administered to five human subjects in three oral and three intravenous experiments. In vivo organ concentrations were measured by gamma ray scintigraphy with computerized area integration, and by whole body counting. Urine was analyzed by solvent separation, and thin layer chromatography of dansylated metabolites. The urine contained less than 5% radiobromine precipitable by acidic AgNO3, demonstrating that the Br label remained organically bound. Solvent separation of urine showed 81.8% of metabolites to be aqueous soluble and 12.5% free base; slower whole body excretion correlated with higher levels of free base in the urine. 14 references. (Author abstract modified)

216789 Jus, Andrzej; Jus, Karolina. Hopital St-Michel-Archange, Quebec 5 **/The biochemical bases of psychopharmacology./** Les bases biochimiques de la psychopharmacologie. Vie Medicale au Canada Francais (Quebec). 4(3):207-211, 1975.

An attempt is made to establish a link between the biochemical action of therapeutic methods and therapeutic effectiveness, based on examples of schizophrenia, affective psychoses and anxiety states. The increase of brain dopamine turnover connected with the antipsychotic effect of neuroleptic drugs, changes in serotonin metabolism in bypolar depression, changes in dopamine metabolism in depressions with motor retardation, and the role of beta-receptor overactivity in anxiety states are discussed. 31 references. (Journal abstract modified)

217204 Cervenka, J.; Bastecky, J.; Kovarik, J. Department of Obstetrics and Gynaecology, Charles University, Londynska 41, 120 00 Prague 2, Czechoslovakia **Psychotropic drugs and ovarial cycle alterations.** Activitas Nervosa Superior Prahal. 16(3):212, 1974.

A paper presented at the 16th Annual Psychopharmacological Meeting, reports a study in which 900 women were examined by a gynecologist in the course of genetic examinations of families with a presence of inborn developmental defects; 750 of them had to be treated for alterations of ovarian

cycles (normoestric anovulation cycles and insufficient lutein phases). In 120 of these 750 women treated with hormones, depression, anxiety, fear of pregnancy and other neurotic symptoms occurred. These patients were ordered diazepam in average daily dose of 15mg and chlorpromazine in average daily dose of 50mg. Normalization of ovaria functions was achieved with the chlordiazepoxide treatment only. In another group of 88 women suffering from lutein insufficiency and hypoestrogeninism, hormonal treatment was not successful.

217258 Rysanek, K.; Benesova, O.; Spankova, H. Medical Clinic, J. E. Purkyne University, Brno, Czechoslovakia **Comparison of the effects of tetracyclic and tricyclic antidepressants on the serotonin uptake by human thrombocytes in vitro.** Activitas Nervosa Superior (Praha). 16(4):307-308, 1974.

The effects of maprotiline and tricyclic antidepressants on the uptake of serotonin by human platelets from healthy Ss were examined. The results indicate that the tetracyclic antidepressant maprotiline differs substantially from classical tricyclic antidepressants. Maprotiline reveals insignificant activity with regard to serotonin uptake inhibition, and interferes with the metabolism of serotonin turnover rate. It is concluded that this in vitro study should be extended to experiments in vivo. 6 references.

217356 Edwards, David J.; Burns, Michael O. University of Pittsburgh School of Medicine, Pittsburgh, PA, 15261 **Effects of tricyclic antidepressants upon human platelet monoamine oxidase.** Life Sciences (Oxford). 15(12):2045-2058, 1974.

The effect of tricyclic antidepressant drugs on human platelet monamine oxidase (MAO) activity was studied. Amitriptyline exhibited noncompetitive inhibition with the substrates phenylethylamine and tryptamine but competitive inhibition with benzylamine. Solubilization and partial purification of platelet MAO did not alter the inhibitory effects of tricyclics. Treatment of the partially purified enzyme with the chaotropic agent sodium perchlorate produced only a slight increase in the inhibition constant for amitriptyline. Findings suggest that selective inhibition of phenylethylamine oxidation may mediate the antidepressant actions of tricyclics. Some evidence is provided for the existence of multiple catalytic sites of MAO activity in the human platelet. 33 references. (Author abstract modified)

217689 Richter, Anna; Smith, S. E. Department of Pharmacology, St. Thomas's Hospital Medical School, London, S. E. 1, England **Inhibition of human platelet 5-hydroxytryptamine uptake by beta-phenethylamine derivatives.** Journal of Pharmacy and Pharmacology (London). 26(10):763-770, 1974.

Forty eight derivatives of beta-phenethylamine were studied as inhibitors of 5-hydroxytryptamine uptake by human blood platelets in vitro. Inhibitory potency was found to be increased by parasubstitution with electronegative groups, by alpha-methylation in the D-configuration and by addition of N-alkyl groups, and to be reduced by saturation of the ring, by ortho-methoxylation, meta-hydroxylation or beta-hydroxylation and by hydrazine formation. It is suggested that optimal affinity involves folding of the molecule to fit a cleft like carrier site. The structural requirements for activity show features of similarity to those of tryptamine and tricyclic antidepressant derivatives and some resemblance with requirements for inhibition of the adrenergic uptake mechanism of the heart. No obvious correlation exists between the activity of these drugs as inhibitors of platelet 5-hydroxytryptamine uptake and their ability to exert effects thought to involve central tryptaminergic mechanisms. 30 references. (Author abstract)

217878 Widman, M.; Agurell, S.; Ehrnebo, M.; Jones, G. Faculty of Pharmacy, University of Uppsala, Box 579, S-751 23 Uppsala, Sweden **Binding of (+)-amphetamine and (-)-delta1-tetrahydrocannabinols and (-)-7-hydroxy-delta1-tetrahydrocannbinol to blood cells and plasma proteins in man.** Journal of Pharmacy and Pharmacology (London). 26(11):914-916, 1974.

The binding of (+)-delta1-tetrahydrocannabinol (THC), (-)-delta1-THC, and (-)-7-hydroxy-delta1-THC to blood cells and plasma proteins was examined in man. All compounds are highly bound with a total binding of 97-99% to the plasma proteins. The distribution of the compounds in whole blood showed a binding to the red blood cells of only 9-10%. When the cannabinoids were incubated with washed red blood cells in the absence of plasma proteins they showed an extensive binding to the cells. These results indicate that in a cannabis smoker most of the THC in blood is present in the plasma and is associated there with the proteins. 13 references.

218153 Merlis, Sidney; Koepke, Hans H. Central Islip Psychiatric Center, Central Islip, NY **The use of oxazepam in elderly patients.** Diseases of the Nervous System. 36(5, Section2):27-29, 1975.

The use of oxazepam in geriatric patients is discussed with reference to metabolic and physiological properties which differentiate oxazepam from other benzodiazepines. The indications of a lack of drug accumulation, the limited degree of drug interaction, the relatively decreased incidence of side-effects and its possible lesser potential for abuse along with its effectiveness in relieving nighttime restlessness suggest that oxazepam can be used on a broader scale than heretofore has been the case. 22 references. (Author abstract modified)

218971 Feinstein, Robert; Gooden, Brett A.; Wolf, Stewart. Marine Biomedical Institute, 200 University Boulevard, Galveston, TX 77550 **The effect of alcohol and barbiturate on the frequency of atrial and ventricular premature beats during sleep.** Pavlovian Journal of Biological Science. 10(2):102-111, 1975.

Measurable findings in man relevant to the likelihood of sudden death during sleep were sought. Repeated electroencephalogram (EEG) and electrocardiogram (ECG) monitoring during sleep was conducted in two Ss with ischemic heart disease and one healthy control. The distribution of ectopic beats among the stages of sleep was ascertained, and the effect of alcohol and barbiturates on the frequency of premature beats was assessed. It was found that neither atrial nor ventricular premature beats favored a particular sleep stage. Neither drug had a consistent effect on their frequency and there was no correlation with heartrate. Premature beats were fewer on the second night of a procedure although a day filled with anxiety greatly increased the frequency of premature contractions. 11 references. (Author abstract modified)

219503 Oksenkrug, G. F. Laboratoriya psikhofarmakologii, Leningradskogo nauchno-issledovatel'skogo psikhonevrologicheskogo instituta im. V. M. Bekhtereva, Leningrad **/Similarities of the influence of secondary and tertiary tricyclic antidepressants on the effect of reserpine in frogs and on the serotonin uptake of human thrombocytes./** Skhodstvo vo vliyanii vtorichnykh i tretichnykh tritsiklicheskikh antidepressantov na effekty rezerpina na lyagushke i pogloshcheniye serotonina trombotsitami cheloveka. Farmakologiya i toksikologiya (Moskva). 38(1):23-25, 1975.

The influence of secondary and tertiary tricyclic antidepressants on the effect of reserpine in frogs and on the uptake of serotonin by human thrombocytes was studied. Imipramine and amitriptyline were the tertiary tricyclic antidepressants; dimethylimipramine and nortriptyline were the secondary tricyclic antidepressants. Both the secondary and tertiary tricyclic antidepressants were found to potentiate the effect of reserpine in frogs and to inhibit the uptake of serotonin by human thrombocytes. Imipramine had a stronger effect than a corresponding dimethylated analog. 6 references. (Journal abstract modified)

219510 Arushanyan, E. B. Chitinskogo meditsinskogo instituta, Chita, U.S.S.R. **/Neurochemical and neurophysiological mechanisms of the psychostimulating action of phenamine./** Neyrokhimicheskiy i neyrofiziologicheskiy mekhanizmy psikhstimuliruyushchego deystviya fenamina. Farmakologiya i toksikologiya (Moskva). 38(1):111-120, 1975.

Current research on the psychostimulating nature of phenamine is reviewed. Specific topics include: the correlation between phenamine and central adrenergic transmissions; phenamine and locomotor activity; localization of phenamine action; phenamine influence on presynaptic terminals; phenamine induced disturbances of noradrenaline accumulation; the effect of phenamine on the perception of various sensory signals; phenamine induced excitation of the mesencephalic reticular formation and individual limbic structures. 232 references.

219630 Raaflaub, J. Dept. of Experimental Medicine, F. Hoffmann-La Roche & Co., Ltd., CH-4002 Basel, Switzerland **On the pharmacokinetics of chlorprothixene in man.** Experientia (Basel). 31(5):557-558, 1975.

To extend the findings on the pharmacokinetics of the drug chlorprothixene, the chlorprothixene blood levels after a single oral or intravenous 30mg dose administered to three human subjects were studied. The half-life during the beta phase of chlorprothixine elimination is of medium magnitude (8-12 hours). The total volume of distribution is very large, indicating a high dispersion of the drug into the tissues; also the values of the total clearance are remarkably high. 10 references.

220973 Lemberger, Louis; Crabtree, Ross; Rowe, Howard; Clemens, James. Indiana University School of Medicine, Indianapolis, IN **Tetrahydrocannabinols and serum prolactin levels in man.** Life Sciences (Oxford). 16(8):1339-1343, 1975.

In a study of tetrahydrocannabinols (THC) and serum prolactin levels in man, delta9-THC, 11-OH-delta9-THC or placebo was administered to casual marihuana smokers in a double-blind, crossover study. Both drugs produced marked pharmacologic and psychologic effects (tachycardia, increased symptom socre and psychologic high). In contrast to effects produced by many other centrally acting drugs, the acute administration of these cannabinoids was devoid of any significant effect on prolactin secretion as determined by monitoring changes in serum prolactin levels. 18 references. (Author abstract)

221386 Siomopoulos, V. Illinois State Psychiatric Institute, 1601 West Taylor Street, Chicago, IL 60612 **Cocaine, amphetamine, and tricyclic antidepressants and synaptic transmission.** Lancet (London). No. 7913:988-989, 1975.

The suggestion in a previous article that convulsive effects observed with repetitive administration of subconvulsant doses of cocaine is related to a pharmacological kindling of the limbic system is refuted. It is more likely that these findings can be explained by cocaine's well known effects on synaptic transmission. Other drugs besides cocaine which enhance adrenergic transmission by preventing the reuptake of norepinephrine by the nerve terminals are amphetamines and tricyclic antidepressants. 4 references.

221538 Gerlach, Jes. Kobenhavns Kommunehospital, Neuromedicinisk afd., DK-1399, Copenhagen, Denmark **/Clozapine: pharmacology, biochemistry and clinical use./** Clozapin: farmakologi, biokemi, og klinik. Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 29(2):93-102, 1975.

Clozapine (Leponex), a new antipsychotic drug, is described. Unlike other neuroleptics, clozapine only produces catalepsy and stereotypy antagonism in extremely high doses, and only when intrastriatally applied. Biochemically, clozapine increases the synthesis and storage of dopamine; at a lower dosage level the release and metabolism of dopamine are unaffected, possibly reduced. Clozapine inhibits the dopamine sensitive adenyl cyclase, which is localized to the postsynaptic receptor membrane. Clozapine blocks the noradrenergic receptor membrane and has a central anticholinergic effect. In controlled clinical studies clozapine's effect has been found equal to or better than levomepromazine, thioridazine, chlorpromazine, and haloperidol. No neurological side-effects are induced; no signs of dopaminergic hypersensitivity are observed after discontinuation. Clozapine's side-effects include initial sedation, persistent hypersalivation and tachycardia. 35 references. (Author abstract modified)

221628 Nagy, Adam; Johansson, Rustan. Klinik II, Lillhagens sjukhus, 422 03 Hisings Backa, Sweden **/Pharmacokinetics of imipramine./** Imipraminets farmakokinetik. Nordisk Psychiatrisk Tidsskrift (Hisings Backa). 28(6):431-432, 1974.

The pharmacokinetics of imipramine were investigated in an experiment which measured the concentration of imipramine in the plasma and blood cells of five subjects. Ss received single doses of imipramine intramuscularly (50 mg), orally (75 mg), and intravenously (25 mg) in that order, and also administered a single dose of desipramine intramuscularly. Oral imipramine was found to be quite poorly utilized in patients with high demethylation capacity during the medicine's first circulatory course. 3 references.

221629 Axelsson, Rolf; Martensson, Erik. no address **On the pharmacokinetics of thioridazine.** Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(6):433-438, 1974.

One hundred and sixty nine psychiatric patients on long-term treatment with thioridazine were studied to determine factors influencing the serum concentration of thioridazine. The rate of elimination of the drug from serum was estimated, and for some patients the serum concentrations of nonconjugated metabolites were determined. A positive correlation was found between the daily doses of thioridazine and the serum concentration up to a daily dose of 6 mg/kg. At higher doses there was a leveling off of the dose - serum concentration relation. Rate of elimination tended to decrease with increasing age. Study of the metabolic pattern suggests that at least part of the pharmacological effect of thioridazine is caused by its metabolically formed sulfoxide. This shows the value of determining metabolites when correlating the serum concentration of thioridazine with its clinical effects. 3 references.

221630 Hansen, C. Eggert. Afd. 0, Statshospitalet, Dk-2600 Glostrup, Denmark **/Pharmacokinetics of perphenazine./** Per-

fenazins farmakokinetik. Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(6):439-440, 1974.

The pharmacokinetics of perphenazine were studied in drug trials with perphenazine hydrochloride and perphenazine-enanthate. Perphenazine hydrochloride in humans was found to have a relatively short half-life in plasma of about 7 hours. Perphenazine-enanthate in intramuscular administration of 100 mg shows depository action with protracted release of perphenazine, but this release may occur too quickly during the first 2 days following ingestion. 2 references.

221631 Forsman, Anders; Ohman, Rolf. Dept. of Psychiatry III, Univ. of Goteborg, Lillhagen's Hospital, 422 03 Hisings Backa, Sweden **On the pharmacokinetics of haloperidol.** Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(6):441-448, 1974.

The pharmacokinetics of haloperidol, a neuroleptic of the butyrophenone type, were explored using a new specific gas chromatographic technique for determining serum haloperidol. The results of these applications are presented together with preliminary data from studies on protein binding and metabolism, absorption, metabolism and excretion of haloperidol. Preliminary data suggest that the capacity to metabolize haloperidol may decrease with advancing age, and that a therapeutic concentration of haloperidol is probably 2-4ng/ml serum. The one to tenfold differences in serum concentrations observed in patients on a standard dose of haloperidol indicate large interindividual differences in the turnover of the drug. Since active metabolites are most likely not formed from haloperidol, the clinical effect of haloperidol probably varies directly with its serum concentration. Interindividual variation in metabolizing haloperidol may result in inadequate medication. 16 references.

221632 Hansen, Lars Bolvig; Kragh-Sorensen, Per. Statshospitalet i Glostrup, Afd. 0, DK-2600 Glostrup, Denmark **/Research into the interaction between nortriptyline and perphenazine -- clinical evaluation./** Undersogelser over interaktionen mellem nortriptylin og perferenazin -- klinisk vurdering. Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(6):449-450, 1974.

The interaction of perphenazine (PPZ) and nortriptyline (NT) was examined in a clinical trial with six patients. No pharmacokinetic interaction occurred at the low dosage of PPZ (4 mg. t.i.d.)used, which resulted in rather low plasma concentrations of PPZ (0.5-1.4micrograms). It is concluded that the interaction between NT and PPZ is dependent on the plasma concentration of PPZ. 4 references. (Author abstract modified)

221648 Riess, W.; Dubey, L.; Funfgeld, E. W.; Imhof, P.; Hurzeler, H.; Matussek, N.; Rajagopalan, T. G.; Raschdorf, F.; Schmid, K. Pharmaceuticals Division, CIBA-GEIGY, Basel, Switzerland **The pharmacokinetic properties of maprotiline (Ludiomil) in man.** Journal of International Medical Research (Northampton). 3(Suppl. 2):16-41, 1975.

An investigation of the pharmacokinetic properties of maprotiline (Ludiomil) in man was reported at the Ludiomil Symposium, Stratford-upon-Avon, England, June 1974. Following intravenous administration of 14C labelled maprotiline in man, 57% of the dose within 21 days was found in the urine and 30% in the feces. The average apparent biological half-life of the unchanged maprotiline in blood was found to be 43 hours. Following oral administration, the dose is absorbed totally, irrespective of size. During repeated administration the concentration profile in the blood attains a steady state after about 7 days. At steady state the peak and minimal concentrations remain at a constant level irrespective of the number of successive doses. These levels are directly proportional to the daily dose administered. Eighty eight percent of the cases recorded gave steady state blood levels between 100ng/ml and 400ng/ml. Six percent each lie above and below these limits. 5 references. (Author abstract modified)

221724 Bente, D.; Matejcek, M.; Penning, J.; Schenk, G. Freie Universitat Berlin, Abt. fur Psychophysiologie, 1 Berlin 19, Nussbaumallee 32-38 **/Spectral analysis of human EEG changes induced by Etifoxin./** Spektralanalytische Untersuchungen zur Wirkung von Etifoxin auf das menschliche EEG. Arzneimittel-Forschung (Aulendorf). 25(6):944-947, 1975.

A spectral analysis of electroencephalographic changes induced in healthy volunteers by Etifoxin, the hydrochloride of 6-chloro-4-methyl-1-phenyl-2-ethylamino-4H-3,1-benzoxazine (Hoe-36801), is reported, in which an oral dosage of 100mg has a differential effect in function of the individual alpha organization. This differential effect appearing in the course of the quantitative evaluation is interpreted as an expression of various partial phases and patterns of a process leading to reduced vigilance. 7 references. (Journal abstract)

221732 Carenzi, Angelo; Gillin, J. Christan; Guidotti, Allesandro; Schwartz, Michael A.; Trabucchi, Marco; Wyatt, Richard J. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, WAW Bldg., Washington, DC 20032 **Dopamine-sensitive adenylyl cyclase in human caudate nucleus: a study in control subjects and schizophrenic patients.** Archives of General Psychiatry. 32(8):1056-1059, 1975.

The effects on striatal adenylyl cyclase activity of several brain metabolites and psychoactive medicines were assessed in autopsied human brain. Striatal adenylyl cyclase activity is selectively stimulated by low concentrations of dopamine. Under the experimental conditions used, norepinephrine was about three times less potent than dopamine. Histamine and serotonin were ineffective. The stimulatiôn by domapine was competitively inhibited by haloperidol. There was no difference between the basal adenylyl cyclase activity or its level after dopamine stimulation between nine control Ss without a psychiatric history and seven patients with chronic schizophrenia. 11 references. (Author abstract)

221821 Kirk, Lars; Ejsing, Lars Ole. Engholmsvej 27, 4000 Roskilde, Denmark **/Metformin (Glucophage) in the treatment of drug-induced obesity./** Metformin (Glucophage) til behandling af medikamental adipositas: en negativ pilotundersogelse. Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(7):533-537, 1974.

Metformin (Glucophage) was tested in five patients with obesity attributed to treatment with lithium and neuroleptic drugs to determine if it encouraged weight loss. The average dose was 3 grams; treatment time was 6-12 months. Average weight loss was 2.6kg. in the first 3 months, followed by no later weight change. Weight differences could be explained by change in body liquid and food intake. Routine blood tests for sugar showed no change through the treatment period. In the long run, Metformin seems to be of little value in treating patients with drug induced obesity. 12 references. (Author abstract modified)

224378 Wolpert, Arthur; Farr, David. Central Islip Psychiatric Center, Central Islip, NY 11722 **Psychotropics and their effect on the EKG in children.** Diseases of the Nervous System. 36(8):435-436, 1975.

The effects of phenothiazines and other psychotropic agents on the EKGs of young, emotionally disturbed children are examined. Fifty consecutive admissions were selected from a children's psychiatric hospital who were examined in detail at the time of admission by the psychiatric, neurologic, pediatric and psychological staff. Of the 50, 36 children were eventually placed on oral, liquid, or tablet medication for a period of at least 1 month. The dose ranges when extrapolated on the milligram per kilogram basis are in the ranges usually associated with EKG abnormalities in adults. None of the EKGs which were taken at a nonfasting condition were reported showing any abnormalities by the consulting cardiologist. No firm explanation for the complete lack of any repolarization changes is offered except perhaps the small sample size. It is possible that the myocardial response to the psychotropics differs in young children or the metabolic breakdown of the chemicals varies from adults. 6 references.

224644 Ichinowatari, Naomichi; Hara, Tsunekatsu; Tanaka, Takao. Department of Mental Hygiene, Ryukyu University, Okinawa, Japan **A clinical study of serum concentration levels of phenobarbital derived from primidone (musoline).** Kyushu Neuro-psychiatry (Fukuoka). 20(3,4):199-205, 1974.

The serum concentration levels of phenobarbital were studied in 14 female psychiatric patients who were treated with primidone. The time lags in the 14 cases until derived phenobarbital appeared in the serum were various, and the shortest one was 7 days after the beginning of primidone treatment. The longitudinal serum concentration levels of the derived phenobarbital in each patient were not constant, and in five patients it increased during menstruation and in two patients it decreased. Five patients had side-effects, such as dizziness, loss of appetite and general fatigue a few hours after beginning of primidone treatment, and the side-effects disappeared several days after termination of primidone treatment when derived phenobarbital was not observed in the serum in any patient. 17 references. (Journal abstract modified)

224773 Garver, David L.; Pandey, Ghanshayam N.; Jones, Frank D.; Dekirmenjian, Haroutune; Hengeveld, Carol T.; Davis, John M. Illinois State Psychiatric Institute, Chicago, IL **Growth hormone release and catecholamines in affective disease.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (P. 98-99).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, May 1975, a paper was presented which reported a study of growth hormone release and catecholamines in patients with affective disorders. Preliminary data suggested an attenuation of insulin induced hypoglycemia (IH), which also induces release of human growth hormone (HGH) by the anterior pituitry, in bipolar depressed patients of various ages and sex. Euthamic and manic bipolar patients had IH induced HGH responses greater than 40ng/ml. In contrast, a heterogenous group of young unipolar depressed patients showed HGH peaks 13.5to greater than 40ng/ml. Apomorphine induced HGH response was variable across affective disease categories, but lowest values occurred in the bipolar group. Urinary 3-methoxy-4-hydroxyphenethylene glycol (MPHG), a product of central noradrenaline metabolism, was measured in 24 hour urines during free periods prior to neuroendocrine testing. In the bipolar Ss, urinary MPHG correlated with IH induced HGH response and with affective state. Finally, the disparate findings of other research were discussed in relation to interaction of age, sex, hypoglycemic response and diagnostic subtypes of affective disease. (Journal abstract modified)

224795 Fink, Max; Irwin, Peter. Health Sciences Center, State University of New York, Stony Brook, NY 11790 **EEG and blood level relations of psychoactive drugs.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 128).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, a paper was presented reporting results of examination of the blood level and electroencephalogram (EEG) relationships for psychoactive drugs. Specifically, the relations between blood levels and EEG were studied for effects of three benzodiazepines, diazepam, bromazepam, and ORF-8063. A continuous blood level - EEG relationship was defined for these compounds. For one compound, ORF-8063, the relationship was stronger for the metabolite than for the drug itself. A current study was described which examines the blood level and EEG relationships for a tetracyclic thymoleptic compound, mianserin (GB-94). (Journal abstract modified)

224800 Huey, Leighton; Janowsky, David S.; Sternbach, Richard. Department of Psychiatry, University of California, San Diego School of Medicine, La Jolla, CA **Neurotransmitter alterations and chronic pain.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 133-134).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, a paper was presented reporting results of a series of studies to determine the effects of various neurotransmitter alterating substances on chronic pain in man. The effects of the serotonin reuptake blocking agent, chlorimipramine, serotonin precursors tryptophan and 5-hydroxytryptophan, and monoamine depleting agent reserpine were investigated in six patients using a double-blind crossover design with matched placebos and active drugs. Results indicate that monoamine depletion caused increased reported pain in chronic pain patients. Addition of serotonin precursors to a chronic pain patient's regime did not have analgesic effects. Chlorimipramine, a serotonin uptake blocking agent, had no amalgesic effects. Findings suggest that neurotransmitter alteration in man may effect chronic pain perception as it does in animals. (Journal abstract modified)

224830 Gottschalk, Louis A.; Dinovo, Eugene; Biener, Robert; Noble, Ernest P.; Birch, Herman. Department of Psychiatry and Human Behavior, College of Medicine, University of California, Irvine, CA **Pharmacokinetics of chlordiazepoxide, meperidine, thioridazine, and mesoridazine and clinical response.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 164-165).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, a paper was presented reporting pharmacokinetic studies of single, standardized, oral or intramuscular doses of chlordiazepoxide, meperidine, thioridazine and mesoridazine. Multiple and continuous dose studies of the thioridazine treatment of acute schizophrenic patients were carried out following single dose administration using either a single dose oral thioridazine (4mg/kg) or intramuscular dose of mesoridazine (2mg/kg). Results showed that there was a predictive relationship between certain of the single dose pharmacokinetic variables and the drug plasma levels achieved with continuous and

prolonged dosage with oral thioridazine. Those patients with the more marked clinical improvement with the single dose tended to improve more rapidly under the multiple and continuous dose regimen. Implications of findings for clinical psychiatric management with the administration of psychopharmacological agents were discussed. (Journal abstract modified)

224832 Rivera-Calimlim, Lenore; Nasrallah, Henry; Strauss, John S.; Lasagna, Louis. University of Rochester School of Medicine, New York, NY **Significance of plasma chlorpromazine in management of psychiatric patients.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 166).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, a paper was presented reporting results of a pilot study which suggested: that psychiatric patients receiving oral chlorpromazine would not improve if only low plasma levels were reached; that those in whom high plasma levels were attained would improve; and that whose who reached very high levels would show toxic side-effects. Administration of trihexyphenidyl appeared to lower plasma chlorpromazine. To evaluate the importance of these findings, the sensitive gas - liquid chromatography assay for plasma chlorpromazine developed with a larger group of patients was used, along with clinical assessment techniques of proven reliability. Findings regarding the effect of trihexyphenidyl on plasma chlorpromazine and the correlations between plasma chlorpromazine and symptom change were reported. (Journal abstract modified)

224909 El-Yousef, M. Khaled; Manier, Hal. University of Southern Florida College of Medicine, Tampa, FL **Tricylcic effect on butaperazine plasma level.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 255-256).

At the 128th Annual Meeting of the American Psychiatric Association, California, Anaheim, May 1975, a paper was presented reporting the effects of desmethylimipramine (DMI) on the butaperazine plasma levels in 17 inpatient schizophrenics. Significantly higher plasma butaperazine levels were measured in Ss receiving 150mg/day of DMI, and more significant increases in levels were noted with higher DMI doses, suggesting a dose dependent effect. Results imply a primary tricyclic effect independent of phenothiazine presence, and its occurrence in only two Ss, who showed activation of psychotic symptoms with the tricyclic despite elevation of plasma butaperazine levels, and reverted after discontinuation of the tricyclic, remains unexplained. The increase in the phenothiazine plasma levels with the tricyclic is not known to the clinician and could influence the clinical efficacy and side-effects of the phenothiazine. The concomitant increase in the blood levels of a phenothiazine such as butaperazine could well be the factor responsible for the clinical response noted in the withdrawn, depressed schizo-affective schizophrenic. (Journal abstract modified)

225058 Costa, E.; Guidotti, A.; Mao, C. C.; Suria, A. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **New concepts on the mechanism of action of benzodiazepines.** Life Sciences (Oxford). 17(2):167-185, 1975.

Evidence is reviewed which suggests that the action of diazepam is mediated by gamma-aminobutyric acid (GABA), establishing a unified concept to explain various reports which indicate that diazepam slows down the turnover rate of catecholamines, serotonin and acetylcholine. These actions require relatively high doses of diazepam and may be explained by assuming that this drug, by acting on regulatory GABA neurons can influence the activity of several neuronal systems in the central nervous system. Findings suggest a role of GABA neurons in anxiety and other symptoms of neurosis for which diazepam is presently the remedy of choice. 59 references.

225062 Noble, Rudolf E. 1801 Bush St., San Francisco, CA 94109 **Galvanic skin resistance (GSR) measurements on volunteers receiving fenfluramine or d-amphetamine.** Current Therapeutic Research. 18(2):338-345, 1975.

Galvanic skin resistance (GSR) measurements were recorded on 12 healthy female volunteers receiving either fenfluramine (20mg x 3) or dextroamphetamine sulfate (5mg x 3) over a 6 hour period in a double-blind study. Absolute levels of GSR were measured every 30 min, starting 1 hour prior to the administration of the first dose (control period) and for an additional 8 hours (treatment period). A comparison of the ratio of the median of the treatment period values, divided by the median of the control period measurements, presented strong evidence that individuals receiving fenfluramine experienced less sympathetic stimulation than those who received dextroamphetamine. 11 references. (Author abstract modified)

225323 Rosenberg, Michael; Sharpe, James; Hoyt, William F. University of Illinois Eye and Ear Infirmary, 1855 W. Taylor St., Chicago, IL 60612 **Absent vestibulo-ocular reflexes and acute supratentorial lesions.** Journal of Neurology, Neurosurgery, and Psychiatry. 38(1):6-10, 1975.

Reversible loss of vestibulocular reflexes with acute supratentorial lesions is reported in two patients receiving therapeutic doses of anticonvulsant drugs. There was no clinical or angiographic evidence of focal brainstem damage. Absence of vestibulocular reflexes is attributed to a combination of acute cerebral damage and anticonvulsant drugs. The loss of these reflexes in patients with acute cerebral lesions cannot be interpreted as evidence of irreversible brainstem injury. 28 references. (Journal abstract modified)

225523 Okada, F.; Daiguji, M.; Yamashita, I.; Suwa, N. Dept. Psychiatry and Neurology, Hokkaido University School of Medicine, Sapporo, Japan **Elevation of plasma dopamine-beta-hydroxylase activity during mecholyl test.** Biological Psychiatry. 10(3):333-339, 1975.

A study is presented to clarify the dynamics of the sympathetic nervous system in humans during the mecholyl test by measuring plasma dopamine-beta-hydroxylase (D-beta-H) activity which has been postulated as an index of the overall activity of this system. Results of the mecholyl test on 16 healthy young males indicate that plasma D-beta-H activity markedly increased in six males who showed prominent responses of systolic blood pressure to mecholyl. However, plasma D-beta-H activity changed only slightly in 10 males who showed minimal response of systolic blood pressure to mecholyl. Data indicate a close correlation between changes in plasma D-beta-H activity, systolic blood pressure, and pulse volume of plethysmogram. 19 references.

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214015 Gillin, J. Christian; Fram, David H.; Wyatt, Richard J.; Henkin, Robert I.; Snyder, Frederick. Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **L-histidine: failure to affect the sleep-**

waking cycle in man. Psychopharmacologia (Berlin). 40(4):305-311, 1975.

L-Histidine was administered to three patients with intractable narcolepsy, to 4 normal volunteers, and to a patient with progressive systemic sclerosis. No effect was observed on nocturnal electroencephalogram sleep patterns in any of the subjects or on the symptoms of the patients with narcolepsy. These results fail to support the hypothesis that histamine is a waking factor. 21 references. (Author abstract)

214018 Dureman, I.; Norrman, B. Department of Psychology, University of Uppsala, Uppsala, Sweden **Clinical and experimental comparison of diazepam, chlorazepate and placebo.** Psychopharmacologia (Berlin). 40(4):279-284, 1975.

A double-blind clinical evaluation of chlorazepate (dipotassium-7-chloro-5-phenyl-2,2-dihydroxy-3-carboxy-1, 2-dihydro-2H-1,4-benzodiazepine), diazepam and placebo in a patient group of young students, mean age 25 years, is reported. Both drugs were significantly better than placebo and according to global assessment chlorazepate was superior to diazepam. An analysis of the main target symptom revealed better effects of chlorazepate on the following items: anxiety, feeling of muscular tension and gastrointestinal disturbances. With respect to irritability and sleep disturbances both drugs were found to be equally effective. In patients' self-ratings chlorazepate was considered superior to diazepam in giving more alertness and less drowsiness during day time. The results are discussed with reference to pharmacokinetic properties of chlorazepate and diazepam. Performance tests in simulated car driving by healthy volunteers did not demonstrate any significant difference as compared with placebo. The psychophysiological effects, however, are more pronounced after diazepam than after chlorazepate medication. 11 references. (Author abstract)

214750 Nakazawa, Yoichi; Kotorii, Tatayu; Kotorii, Makoto; Horikawa, Shuichi; Ohshima, Masachika. Dept. of Neuropsychiatry, Kurume University, School of Medicine, Kurume, Japan **Effects of amitriptyline on human REM sleep as evaluated by using partial differential REM sleep deprivation (PDRD).** Electroencephalography and Clinical Neurophysiology (Amsterdam). 38(5):513-520, 1975.

The suppressant effect of amitriptyline on rapid eye movement (REM) sleep and the capacity of the drug to produce REM rebound were investigated using electroencephalographic recordings from five normal subjects. Administration of a single 25 mg dose of amitriptyline 30 min. prior to sleep onset was followed by a significant decrease in REM sleep, but not by any distinct rebound elevation in REM sleep during the subsequent 2 recovery nights. The use of a single 25 mg dose of the drug on the day following partial differential REM sleep deprivation (PDRD) was attended by a significant decrease in REM sleep and by a rebound elevation of REM sleep during the following recovery night. The adequacy of the PDRD technique in evaluation of drug effects on sleep is discussed. 23 references. (Author abstract modified)

215058 Murphy, J. E.; Forrest, W. A. Northampton, England **A comparison between maprotiline (Ludiomil) and amitriptyline in the treatment of depressive reaction in general practice.** Journal of International Medical Research (Cambridge). 3(2):108-113, 1975.

Maprotiline (Ludiomil) and amitriptyline were compared in the treatment of depressive reaction in general practice. Findings indicate that maprotiline and amitriptyline, in a fixed dosage regime of 50mg three times daily for 3 weeks, were equally effective therapeutic agents. All but two of the patients improved during the trial. Results indicate that in those patients who completed the trial both compounds were relatively well tolerated. The general pattern of side-effects was similar for both treatments, although maprotiline appeared to cause more dizziness than amitriptyline. 9 references. (Author abstract modified)

215059 Floru, Lucian. Komm. Rheinisches Landeskrankenhaus-Psych. Univ-Klinik, 4000 Dusseldorf, Bergische Landstrasse 2, Germany **Aspects of long-term treatment with neuroleptics: historical and literature review--personal experience with fluspirilene and penfluridol.** Journal of International Medical Research (Cambridge). 3(2):114-124, 1975.

The literature on neuroleptics with substance specific long-term effects (fluspirilene, penfluridol) is reviewed in tabular form. This is followed by a report of personal investigations on 76 schizophrenics who were treated with fluspirilene initially within the hospital and later on an outpatient basis and on 86 patients who were treated with it exclusively at the outpatients' department, as well as on 123 schizophrenic psychoses treated with penfluridol in the outpatient department. Side-effects caused by the two substances are compared. Prerequisites for effective long-term therapy with a few complications are discussed. 107 references. (Author abstract)

215667 Seppala, Timo; Linnoila, Markku; Elonen, Erkki; Mattila, Mauri J.; Maki, Martti. Department of Pharmacology, University of Helsinki, Helsinki, Finland **Effect of tricyclic antidepressants and alcohol on psychomotor skills related to driving.** Clinical Pharmacology and Therapeutics. 17(5):515-522, 1975.

In a study of psychomotor skills related to driving, 20 healthy subjects took amitriptyline, doxepin, and placebo for 2 wk each in a double-blind crossover trial, and another 20 subjects similarly took nortriptyline, chlorimipramine, and placebo. Dose response graphs for the tyramine pressor effect were shifted to the right during the antidepressant treatment, indicating a blockade of the membrane pump in peripheral sympathetic terminals. Amitriptyline in combination with alcohol increased cumulative choice reaction times, and doxepin in combination with alcohol increased both cumulative choice reaction times and inaccuracy of reactions. Coordination was impaired after both of these combinations on the seventh day. It seems as if doxepin and amitriptyline but not nortriptyline or chlorimipramine, in combination with 0.5gm/kg of alcohol, may be especially dangerous in driving. 20 references. (Author abstract modified)

215673 Sunshine, Abraham. 907 Fifth Ave., New York, NY 10021 **Comparison of the hypnotic activity of triazolam, flurazepam hydrochloride, and placebo.** Clinical Pharmacology and Therapeutics. 17(5):573-577, 1975.

Triazolam, flurazepam and placebo were compared in a double-blind, randomized 5 night crossover study in 25 inpatient insomniacs. These patients all complained of difficulty falling asleep; all said they usually slept less than 5 hr a night and woke up too early in the morning. Results of the patients' global evaluation of the medications shows that all of the treatments were rated significantly higher than placebo, with the exception of triazolam, which was not significantly different from flurazepam, or from placebo. In subjective evaluation of sleep onset, only triazolam was rated faster than placebo while in the objective evaluation of sleep onset only triazolam was rated faster than placebo. All four active medi-

cations increased duration of sleep. Triazolam and flurazepam were rated as providing deeper sleep than placebo while all treatments except flurazepam, decreased the number of awakenings below that on placebo. A significant dose response curve was obtained with triazolam andflurazepam for some of the parameters. 4 references. (Author abstract modified)

215740 Feinberg, Irwin; Jones, Reese; Walker, James M.; Cavness, Cleve; March, Jonathan. VA Hospital, San Francisco, CA **Effects of high dosage delta-9-tetrahydrocannabinol on sleep patterns in man.** Clinical Pharmacology and Therapeutics. 17(4):458-466, 1975.

Electroencephalographic readings and eye movement were recorded in experienced marihuana users under placebo and tetrahydrocannabinol (THC). Four subjects were studied for 3 baseline nights, 3 nights under initial dosage of 70mg/day, the last 3 nights of a 2 wk period of 210mg/day, and the first 3 nights of withdrawal. administration of THC significantly reduced eye movement activity during sleep with rapid eye movements (REM) and, to a lesser extent, the duration of REM itself. Withdrawal led to increases above baseline in both measures but the rebound effect was greater for eye movement. Stage 4 sleep tended to increase on drug, but this effect was not statistically significant. On withdrawal, stage 4 sleep decreased significantly; this change was marked only on the first withdrawal night. Possible relations between effects on sleep pattern and on behavior are discussed. 29 references. (Author abstract modified)

215857 Smith, W. Lynn; Lowrey, Jack B. Cortical Function Laboratories, Porter Memorial Hospital, 2525 South Downing Street, Denver, CO 80210 **Effects of diphenylhydantoin on mental abilities in the elderly.** Journal of the American Geriatrics Society. 23(5):207-211, 1975.

An assessment was made of the effects of diphenylhydantoin (DPH) on the mental functions of clinically normal elderly persons whose basic intelligence levels ranged between normal and bright normal and who represented middle and lower upper socioeconomic groups. Significant increases in favor of DPH were observed in the Information, Comprehension, and Digit Symbol subtests of the Wechsler Intelligence Scale (WIS), and in the Verbal Scale and Full Scale Intelligence Quotients of the WIS. The first two measures indicated significant improvement in long-term memory and social comprehension. The third reflected an increase in the ability to learn new material and increased speed in the visual motor coordination. The fourth and fifth showed the effectiveness of DPH in improving general mental functioning. Apparently the underlying factor synthesizing these general DPH associated improvements is mental concentration. 6 references. (Author abstract modified)

215955 Okuma, Teruo; Hata, Naoyuki; Fujii, Shozo. Department of Psychiatry, Tohoku University School of Medicine, Sendai, Japan **Differential effects of chlorpromazine, imipramine, nitrazepam and amobarbital on REM sleep and REM density in man.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 29(1):25-37, 1975.

The effect of chlorpromazine (CPZ), imipramine (IMP), nitrazepam (NZP) and amobarbital sodium (AMOB) on the rapid eye movement period of sleep (REMP) was investigated. CPZ 25mg resulted in a slight increase in %REMP, and no significant change in REM density and total REM activity during the drug and withdrawal nights. IMP 25mg produced moderate decrease in %REMP in the three drug nights, whereas REM density decreased only in the first drug night. NZP 5mg resulted in a slight and parallel suppression of %REMP, REM density and total REM activity during the drug nights. AMOB 200mg produced a slight decrease in %REMP and a marked decrease in REM density during the drug nights. Rebound increase of %REMP and a tendency to carry over decrease of REM density were observed in the withdrawal nights. The importance of the simultaneous analysis of %REMP and REM density in psychotropic drug sleep research is emphasized. 42 references. (Author abstract modified)

216902 Richou, H.; Hug, R. Institut Marcel-Rivier, 78320 La Verriere, France **/Oral contraception and induced depressive states./** Contraception orale et etats depressifs induits. Annales Medico Psychologiques (Paris). 2(1):203-208, 1974.

Depression observed in women taking oral contraceptives is reviewed. A number of researchers have found a rather high incidence of depressive states among women taking the pill. Most depressive disturbances are directly a function of increased progesterone levels. The essential precaution is to avoid the use of pills containing a large amount of progesterone.

217000 Kleyn, M.; Sobor, A. Nervnoye otdeleniye, Rayonnoy bol'nitsy XIII rayona, Budapest, Hungary **/A therapeutic study of sidnocarb./** Terapevticheskoye issledovaniye tabletok sidnokarba. Zhurnal nevropatologii i psikhiatrii imeni S. S. Korsakova (Moskva). 75(2):275-278, 1975.

The therapeutic effectiveness of sidnocarb was investigated in 30 patients with neurasthenia, psychasthenia, hypothalamic syndrome, and depression. The initial dosage was 5mg, 2 times a day, and was gradually increased to 20-30mg/day. The treatment period varied from 3 to 8 weeks. Daily records were made of the patients' psychic and somatic conditions. Sidnocarb proved to have no effect on either hypothalamic syndrome or depression. It was however, somewhat effective in treating both neurasthenia and psychasthenia. No side-effects such as changes in pulse, blood pressure, blood or urine content were observed. Sidnocarb also proved effective when used in conjunction with neuroleptic and antidepressant preparations. (Journal abstract modified)

217003 Obukhov, G. A. no address **/Neuroleptics of prolonged action (a survey of foreign literature)./** Neyroleptiki prolongirovannogo deystviya (obzor inostrannoy literatury). Zhurnal nevropatologii i psikhiatrii imeni S. S. Korsakova (Moskva). 75(2):285-295, 1975.

Research on neuroleptics with prolonged action capabilities is reviewed. The action of the neuroleptics studied has been prolonged either by changing the content of the drug, or by changing its form to one that will be absorbed very slowly by the body. Details of the experiments, effectiveness and side-effects of the following neuroleptics are given: fluphenazine; fluphenazine enanthate, fluphenazine decanoate, pimozide, fluspiriline, and penfluridol. 263 references.

217041 James, N. McI.; Montague, Anne F. Ashburn Hall, Dunedin, New Zealand **A double blind trial of nitrazepam and flurazepam as sedatives.** New Zealand Medical Jounral (Dunedin, New Zealand). 81(535):246-248, 1975.

A double-blind crossover trial was conducted using flurazepam and nitrazepam as sedatives in a group of a dozen psychiatric inpatients. The results show highly significant differences between effects of placebo and those of active drugs. The differences between the two drugs were not significant, apart from the subjective estimate of time slept, in which flu-

razepam was superior. As other studies have confirmed their safety, relative lack of side-effects and very low addictive potential, it is concluded that there is little difference between them, except for the possibility that flurazepam may be preferred subjectively. 17 references. (Author abstract)

217181 Hoffman, Stanley P.; Engelhardt, David M.; Margolis, Reuben A.; Polizos, Polizoes; Waizer, Jonas; Rosenfeld, Roberta. Psychopharmacology Research Unit, S.U.N.Y., Downstate Medical Ctr. 450 Clarkson Avenue, Brooklyn, NY 11203 **Response to methylphenidate in low socioeconomic hyperactive children.** Archives of General Psychiatry. 30(3):354-359, 1974.

Sixty two children from economically deprived urban areas and diagnosed hyperkinetic reaction of childhood were studied in order to evaluate the effects of methylphenidate hydrochloride in this population. Methylphenidate was as effective as it has been reported to be in children from different socioeconomic and cultural settings. Improvement was noted in many areas of the child's functioning, and was observed by parents, teachers, and the treating physician. Results of the study were further analyzed by dichotomizing the children according to the weekly variability in classroom hyperactivity over the 12 week treatment period. It was found that those children whose variability in weekly ratings of classroom hyperactivity was relatively high were seen as more of a problem by their parents at the baseline evaluation than were the children whose treatment response tended to be less variable. 17 references. (Journal abstract)

217205 Hrbek, Jan; Komenda, S.; Macakova, J.; Siroka, A.; Navratil, J.; Medek, A. Department of Pathological Physiology, Medical Faculty of the Palacky University, Olomouc, C.S.S.R. **The effects of scopolamine (0.6 mg) and physostigmine (1.0 mg) on higher nervous activity in man, followed-up during 5 hours after application.** Activitas Nervosa Superior Praha). 16(3):213-215, 1974.

A paper presented at the 16th Annual Psychopharmacological Meeting, reports a study in which the method of artificial conditioned speech connections was adopted following up the performances of 16 volunteers in the process of learning after subcutaneous applications of scopolamine (S), physostigmine (P) combination of both drugs, and placebo. The criteria were the number of repetitions necessary for mastering the given task (NNR), then the number of correct responses (NCR), and the frequency of responses (FR) during the first eight repetitions, when the active knowledge of the experimental subjects was tested. The inhibitory effect of S on the learning process was observed in NNR in the first 4 hours, in NCR in 5 hours, in FR in the fourth and the fifth hour after application. The impairment of performance after S was eliminated by physostigmine. Scopolamine decreased significantly the values of the heartrate from the first up to the fifth hour of its action. 3 references.

217546 Sagales, Teresa; Erill, Sergio. Hospital de la Santa Cruz y San Pablo, Avda. S. Antonio M. Claret 167, Barcelona 13, Spain **Effects of central dopaminergic blockade with pimozide upon the EEG stages of sleep in man.** Psychopharmacologia (Berlin). 41(1):53-56, 1975.

The effect of pimozide, a potent and specific blocker of central dopaminergic transmission, upon the sleep of man was studied in six healthy volunteers. Given at doses of 1 and 4mg, which have clear central effects in humans, pimozide produced only minor changes in the electroencephalogram (EEG) patterns of sleep. At these doses a slight and nonsignificant decrease in phase I sleep was observed, while phases W, II, III, IV and rapid eye movement (REM) were not modified. No differences were noted between drug or posttreatment and control nights in total NREM sleep, total REM sleep, number of episodes of REM or total number of eye movements. An increase in REM sleep in the first third of the second pimozide night and an increase in the duration of the first REM period in the first drug night were the only statistically significant findings. The results suggest that dopamine is, at most, of rather minor importance in the physiology of sleep in man. 23 references.

217548 Vogel, Gerald; Thurmond, Arthur; Gibbons, Pauline; Edwards, Kay; Sloan, Katherine B.; Sexton, Kenneth. Sleep Laboratory, GMHI, 1256 Briarcliff Road, N.E., Atlanta, GA 30306 **The effect of triazolam on the sleep of insomniacs.** Psychopharmacologia (Berlin). 41(1):65-69, 1975.

Circling models for the detection of antiparkinson activity were compared. The effects of three oral doses of bedtime triazolam, a new benzodiazepine, on the laboratory sleep of insomniacs were studied in a double blind design which used the following 14 consecutive night schedule: 1-4 placebo; 5-11 drug; 12-14 placebo. Side-effects or toxic effects were assessed by screening physicals and questionnaires administered each morning and each evening and by a comparison of the prestudy vs. end study physical exams and clinical lab tests. At the 0.5mg dose triazolam significantly reduced several objective and subjective measures of insomnia. It had lesser effects at the 0.25mg dose and equal or greater effects at 1.0mg dose. There were no remarkable side-effects or toxic effects at any dose. 10 references. (Author abstract modified)

217549 Jacob, Rolf G.; Holmstrand, Jan; Eriksson, Jan H.; Anggard, Erik. Psychiatrric Research Center, University of Uppsala, Ulleraker Hospital, S-750 17 Uppsala 17, Sweden **Propranolol in the treatment of opiate dependence -- a controlled study.** Psychopharmacologia (Berlin). 41(1):71-73, 1975.

Two double-blind placebo controlled experiments designed to elucidate the alleged narcotic blocking effect of propranolol were performed. Propranolol 40mg or 20mg was given together with methadone during the acute withdrawal phase of opiate addiction. The second experiment assessed whether 10mg of propranolol, given 2 hrs before 30mg of morphine i.v.,reduced the euphoric effects of the latter drug. In none of the experiments could narcotic blocking effects be detected. The group receiving 40mg propranolol during detoxification exhibited the highest proportion of patients staying for the whole prescribed detoxification period. 7 references. (Author abstract)

217556 Hollister, Leo E. VA Hospital, Palo Alto, CA 94304 **Dose-ranging studies of clonazepam in man.** Psychopharmacology Communications. 1(1):89-92, 1975.

A potent benzodiazepine derivative, clonazepam, was studied over a range of single doses to determine tolerance for the drug. The best tolerated doses were 0.5and 1mg. Higher doses were associated with considerable evidence of sedation, more easily detected by clinical questioning and observation than by commonly used self-reporting scales or motor tests. 2 references. (Author abstract)

217957 Omine, Shigeji; Nishikawa, Kisaku; Kashima, Haruo. Department of Neuropsychiatry, National Chiba Hospital, Japan **Clinical experience of haloperidol injection on psychiatric cases.** Medical Consultation & New Remedies (Tokyo). 11(11):2371-2378, 1974.

The effect of haloperidol injection on schizophrenia and mania was studied. Twenty two patients with schizophrenia and three manic intramuscularly treated with haloperidol for 2-12 days. The effectiveness of haloperidol in alleviating certain symptoms is reported. It is noted that 15 of the 25 patients experienced side-effects, which included tremor, irritation, and drowsiness. The overall effectiveness of haloperidol is confirmed. 7 references.

218118 Werry, John S.; Aman, Michael G. Dept. of Psychiatry, School of Medicine, University of Aukland, Auckland, New Zealand **Methylphenidate and haloperidol in children: effects on attention, memory, and activity.** Archives of General Psychiatry. 32(6):790-795, 1975.

Twenty four hyperactive or unsocialized aggressive children were subjects in an exploratory double-blind crossover study comparing the cognitive effects of methylphenidate hydrochloride (0.3mg/kg), two doses (0.25 and 0.05mg/kg) of haloperidol and inert placebo. Each subject received each of four drug conditions, drug order being randomized by a Latin square design. At the end of each 18 day trial period, attention, immediate recognition memory, reaction times, and seat activity were tested. While drug effects were small, methylphenidate and, to a lesser extent, the low dose of haloperidol, facilitated performance; wereas there was some suggestion that the high dose of haloperidol may have caused a slight deterioration in performance. These results are contrasted with effects on social behavior where the latter improved behavior. No differences attributable to diagnosis were found. 37 references. (Author abstract modified)

218156 Salzman, Carl; Kochansky, Gerald E.; Shader, Richard I.; Harmatz, Jerold S.; Ogletree, Ann M. Psychopharmacology Research Laboratory, Massachusetts Mental Health Center, 74 Fenwood Road, Boston, MA 02115 **Is oxazepam associated with hostility?** Diseases of the Nervous System. 36(5, Section 2):30-32, 1975.

Clinical and research observations on the relationship between oxazepam and hostility are reviewed. In the laboratory, hostile verbal behavior with oxazepam was mildly increased but only after a condition of interpersonal frustration. There are no clinical observations of oxazepam associated with hostile mood states. In the laboratory, oxazepam is associated with a decrease in hostile mood even after a frustration. Results suggest that oxazepam differs from chlordiazepoxide and diazepam with reference to hostility increase, but future applications of these observations must remain tentative. 28 references.

218165 Carcassonne, M. Service de Chirurgie Infantile, C.H.U. Nord, 13015 Marseille, France /**Essential infantile enuresis and Dogmatil.**/ Enuresie essentielle infantile et Dogmatil. Semaine des Hopitaux Therapeutique (Paris). 50(10):697-699, 1974.

The effect of sulpiride (Dogmatil) on infantile enuresis was investigated. Dosage was 5mg/kg in 24 hours. The maximum dose was 10mg/kg. Out of 24 children treated, five presented good results, i.e.,they were perfectly cured. In 11 cases, sulpiride altered the frequency and importance of the enuresis without suppressing it completely. The drug had no effect on eight cases. No side-effects were noted. The drug was also beneficial with respect to psychological behavior, as it stabilized mood and decreased agitation and aggressiveness. It is concluded that sulpiride represents an innocuous means of treating primitive infantile enuresis.

218166 Risberg, Ann-Marie; Risberg, J.; Ingvar, D.-H. Service de Neurophysiologie clinique, Hopital de l'Universite, Lund, Sweden /**Effects of hexapropymate on the sleep of the normal man measured by a polygraphic method.**/ Effets de l'hexapropymate sur le sommeil de l'homme normal mesures par une methode polygraphique. Semaine des Hopitaux Therapeutique (Paris). 51(2):99-104, 1975.

The effects of a normal dose (400mg) of hexapropymate on sleep were investigated by a polygraphic method with 16 healthy volunteers. The results showed that there were only slight differences in the general aspect of sleep between the nights with hexapropymate (H) and the nights with placebo (P), with a weak, but significant, decrease in the total duration of paradoxal sleep which increased to 10.2% of the value obtained for the night with placebo. With the S population studied, it was difficult to establish a very marked effect of the hypnotic agent, since the young tend to be good sleepers. Nevertheless, hexapropymate clearly has a hypnotic effect. A slight increase in the total duration of sleep and a decrease in the latency of sleep and number of nocturnal awakenings were recorded, which were proof of the hypnogenic action of hexapropymate. 16 references.

218214 Moriarty, John D. 7080 Hollywood Blvd, Los Angeles, CA 90028 **Insomnia: often a therapeutic challenge.** Diseases of the Nervous System. 36(5):279-280, 1975.

Insomnia is defined, the prevalence of insomnia in psychiatric patients is discussed, and clinical aspects of insomnia are reviewed. Two types of insomnia are distinguished: 1) difficulty in falling asleep and frequent wakening and 2) early morning wakening. The first group of patients respond well to minor tranquilizers and psychotherapy, whereas the second do well with tricyclic antidepressants. Studies in sleep laboratories delineating the stages of sleep and the importance of rapid eye movement (REM) sleep are briefly discussed, and caution is advised in clinical use of hypnotics which suppress REM sleep and produce a rebound increase on withdrawal. 8 references. (Author abstract modified)

218953 Gaillard, Jean-Michel; Aubert, Claude. Psychiatric University Clinic of Bel-Air/Geneva, CH-1225 Chene-Bourg, Switzerland **Specificity of benzodiazepine action on human sleep confirmed. Another contribution of automatic analysis of polygraph recordings.** Biological Psychiatry. 10(2):185-197, 1975.

The hypothesis that benzodiazepine induced modifications of sleep in human Ss is not a common effect of all psychotic drugs, but rather a specific one, was tested. Each of three drugs tested in equimolar doses, thioridazine, pentobarbital, and oxazepam, induced characteristic effects on sleep. Thioridazine did not affect the quantity of slow wave sleep and of rapid eye movement (REM) sleep. REM sleep latency was significantly shortened, and the number of cycles during the night was increased. Pentobarbital influenced slow wave sleep very slightly, decreased REM sleep, but did not modify the number of rapid eye movements with respect to REM sleep duration. Oxazepam decreased slow wave sleep, REM sleep, and the density of REM sleep, the absolute number of REM being proportionally much more reduced than REM sleep itself. These findings are consistent with the hypothesis. 33 references. (Author abstract modified)

219354 Schain, Richard J.; Reynard, Carol L. Dept. of Pediatrics, UCLA School of Medicine, Los Angeles, CA 90024 **Observations on effects of a central stimulant drug (methylphenidate) in children with hyperactive behavior.** Pediatrics. 55(5):709-716, 1975.

Ninety eight hyperactive children, ages 6-12 years, were treated with methylphenidate (MP) or placebo under double-blind conditions. Only one of the 48 children receiving placebo (2%) was judged to be a drug success, whereas 70% of the 94 children receiving MP were judged to be drug successes at the end of the 12 week period. A wide range of dosage (0.2-1.9mg/kg) was required for optimum drug effects. It is concluded that a trial of stimulant drugs is indicated in hyperactive children manifesting impairment of educational and social progress. Dosage adjustment and judgment of drug success or failure require regular reports from teachers and parents. 28 references. (Author abstract modified)

219836 Scherrer, P.; Maillard, M. no address **/Alcoholism and incisive neurolpetics./** Alcoolomanie et neuroleptiques incisifs. Revue de l'Alcoolisme (Paris). 20(4):261-266, 1974.

Treatment of alcoholism with fluphenazine enanthate, administered i.m. every 3 weeks in 50-75mg doses, is discussed. Case histories of four young women who drank secretly are presented. Ss manifested affective immaturity, character neurosis, and prepsychotic personality traits. Only one of the women was cured by the therapy; another improved sufficiently to allow her to voluntarily use the services of a psychiatric hospital. Seven men were also treated, and after a year of treatment, there were five "cures" out of the seven. Only one was unable to go back to work; he was the oldest of the Ss and presented extrapyramidal disturbances connected with the therapy. In one of the two failures, the patient's mother insisted on terminating treatment. In the other case, the S continued to drink, but was no longer violent toward his family.

220510 Costello, William Henry. University of Montana **The effectiveness of Ritalin and token economy in increasing hyperkinetic children's coloring behavior. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-8236 HC$13.50 MF$5.00 141 p.

The effectiveness of Ritalin and token economy in increasing hyperkinetic children's coloring from a pretest to a posttest condition was examined using a nondeception, split plot factorial design with five experimental groups: Ritalin - token economy, placebo - token economy, no drug - token economy, Ritalin - no token economy, and placebo - no token economy. The 30 hyperkinetic children were observed on a 20 min pretest and posttest coloring task, and had their appropriate medication prescribed by their pediatrician. Parents were assembled into two groups (token and no token economy), independently recorded their children's nightly drawing times, met with E for four group meetings during the 4 week treatment period, and independently rated their children on the Burks' Behavior Rating Scale at pretest and posttest. Results indicate that while Ritalin - token economy Ss showed the largest drawing and coloring times, Ritalin - no token economy Ss showed the smallest drawing and coloring times. The suggestion that Ritalin allows the child to better understand the environmental contingencies around him is discussed, along with implications for hyperkinetic children. (Journal abstract modified)

220523 Firestone, Philip. McGill University **The effects of reinforcement contingencies and caffeine on hyperactive children. (Ph.D. dissertation).** Dissertation Abstracts International. Ottawa, National Library of Canada.

The performances of hyperactive and control children were compared on a delayed reaction time task under three reinforcement conditions: reward, punishment, and reward plus punishment. Hyperactives had slower and more variable reaction times, suggesting an attentional deficit. Although each of the three reinforcement conditions was successful in improving reaction times for both groups, reward led to a significant increase in impulsive responses in the hyperactive children. Autonomic data reveal that reward also increased arousal to a greater extent than punishment or reward plus punishment. Although resting skin conductance was not different in the two groups, hyperactives produced fewer specific autonomic responses to signal stimuli. A second experiment investigated the effects of caffeine on hyperactivity. Although caffeine seemed to improve reaction times and psychological test scores, these differences were not significant. However, impulsivity and general behavior, as measured by teacher and parent rating scales, clearly showed a significant improvement due to caffeine. (Journal abstract modified)

221271 Aschoff, J. C.; Becker, W. Nervenzentrum, Abteilung fur Neurologie der Universitat, 79 Ulm, Steinhovelstr. 9 **/The influence of sulpiride on vigilance: objective measurements of the visuomotor system./** Der Einfluss von Sulpirid auf die Vigilanz: objektive Messungen am optomotorischen System. Arzneimittel-Forschung (Aulendorf). 24(1):2058-2062, 1974.

Changes in the maximum velocity and duration of saccadic eye movements under the influence of sulpiride (Dogmatil) were evaluated by computer. Sulpiride showed no influence on velocity and reaction time and possibly enhances accuracy of saccadic eye movements; sulpiride is recommended for special purposes in aviation and space medicine and can be considered to be safe in normal traffic. The reproducible and time saving computerized method has proven to be useful in evaluating different drugs with respect to their influence on psychomotor performance or changes in vigilance which may be hazardous for traffic safety. 8 references. (Journal abstract modified)

221272 Perbellini, D.; Castellani, A.; Lescovelli, M. Ospedali Neuropsichiatrici Provinciali, Verona-Marzana, Italy **Electroencephalographic study for the evaluation of the effects of 7-chloro-5-phenyl-3H-1,4-benzodiazepine-2-(1H)-one (N-demethyldiazepam) on sleep disturbances in a group of mental patients.** Arzneimittel-Forschung (Aulendorf). 24(1):2062-2066, 1974.

7-Chloro-5-phenyl-3H-1,4-benzodiazepine-2-(1H)-one (N-demethyldiazepam) was administered and sleep modifications were studied electroencephalographically in a group of 20 patients suffering from mental disturbances and having in common varying degrees of sleep disturbance. The drug demonstrated a remarkable and selective efficacy by shortening the sleep onset time, improving the quality of sleep and favoring the appearance of the REM phases. It is concluded that the drug is a good hypnotic, capable of inducing a condition similar to normal sleep. 27 references. (Journal abstract)

221339 Schneider, E.; Ziegler, B.; Maxion, H.; Badawi, M. Abteilung fur Neurologie der Universitat, 6 Frankfurt/Main-71, Schleusenweg 2-16 **/The influence of sulpiride on sleep: results of polygraphic night sleep recordings./** Der Einfluss von Sulpirid auf den Schlaf Ergebnisse kontinuierlicher EEG-Untersuchungen. Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 8(2):90-98, 1975.

Short-term and long-term effects of sulpiride on the sleep electroencephalogram (EEG) in humans were investigated in 8 patients suffering from autonomic instability. In each patient, seven polygraphic night sleep recordings were performed. After an adaptation night and 2 nights without medication, each S got 200mg-400mg sulpiride i.m. for 2 days and then

300mg-600mg orally for a 3 week period. In both groups, the short-term application of sulpiride caused a reduction of waking periods and a slight decrease of stage three, while stage two was increased. In psychotic patients, the long-term orally administered format was followed by an increase of deep synchronous sleep (stage four). As this alteration of sleep could not be discerned in the controls, this finding is a result of the improvement of psychosis. In the patient groups, the amount of REM sleep was augmented during the short-term application as well as during the long-term application, whereas in the control group, the amount of REM sleep decreased when sulpiride was given orally for 3 weeks. Results are compared with those of other drugs. 30 references. (Journal abstract modified)

221634 Muus, P.; Kirk, Lars. no address **/Similarities in the effects of lithium carbonate, Litarex and Lithionite duretter: preliminary study./** Sammenligning af bivirkninger ved Lithii carbonas, Litarex og Lithionit duretter: preliminaer meddelelse. Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(6):455, 1974.

The effects of three lithium preparations, lithium carbonate, Litarex, and Lithionit duretter, were compared in 19 outpatient subjects who had been treated with lithium for at least 6 months. All three preparations were given in 2 week periods. Lithium carbonate was given twice daily, Litarex and Lithonite duretter were given in single evening doses. General effects of fatigue, muscular ache, depression, irritability were light in 8% of the Ss, moderate in 7%, and great in 4%; 26% experienced light tremors; 15% moderate tremors; 11% had mild gastrointenstinal symptoms; thirst was light in 48%, moderate in 16%, and great in 10%. A tendency toward gastrointestinal symptoms with Lithonite duretter was reported, but may not be significant. All patients considered the tablet form of Lithionit duretter good, but 37%-42% had reservations about tablet forms of the two other preparations. The difference here was significant; 58% preferred single doses. It was concluded that all three preparations are useful in treatment.

221664 Nozawa, Akira. Second Dept. of Internal Medicine, School of Medicine, Toho Univ., Ohmori-Nishi 6-11-1, Ohta-Ku, Tokyo, 143 **Studies on microvibration of unidentified clinical syndrome.** Journal of Japanese Psychosomatic Society (Fukuoka). 15(2):106-115, 1975.

In a clinical application of microvibration (MV) to the examination of autonomic function, MV patterns were recorded before and after Mecholyl (methacholine) loading in 51 patients who were suffering from unidentified clinical syndromes. The cases were compared to control subjects, and the relation between MV and various psychological tests (Cornell Medical Index, Yatabe Guilford personality test, Manifest Anxiety Scale, and Self-Rating Questionnaire for Depression) were examined. 20 references. (Journal abstract modified)

221738 Klebel, Edeltraud. Kuratorium fur Verkehrssicherheit, Olzeltgasse 3, A-1031 Wien III, Austria **/Experimental psychological study on the effect of a combination of hexobendine, ethamivan and etofylline./** Experimentalpsychologische Untersuchung der Wirkung einer Hexobendin-Etamivan-Etofyllin-Kombination. Arzneimittel-Forschung (Aulendorf). 25(5):831-836, 1975.

Instenon forte, a combination of hexobendine, ethamivan and etofylline for treatment of cerebral vascular insufficiency, was tested for its effects on performance in driving. The experimental and control groups consisted of male and female Ss, aged 17 to 25 years. All Ss were tested with the same series of psychological tests before and after long-term medication. The male Ss showed moderate increases of concentration performance and short-term memory under Instenon in various tests. Quick comprehension of complex traffic situations was significantly enhanced in the male experimental group, whereas reactive behavior under stress was impaired. In the female experimental group, an increase of focal attention and an improvement of reactive behavior under stress was found, while quick comprehension of complex traffic situations was impaired. The results indicate that neither female nor male Ss demonstrate a consistent positive or negative effect of Instenon on functions related to driving. 19 references. (Journal abstract modified)

222060 Larison, Grey Richard. Michigan State University **The use of free imagery, non-directive interviewing, and selected drugs to lift posthypnotic repression. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-14777 HC$13.50 MF$5.00 236 p.

The use of free imagery, nondirective interviewing, and selected drugs to posthypnotic repression was studied using Reyher's posthypnotic conflict paradigm as the research model. This model is effective in hypnotically implanting a conflict to which the S then posthypnotically responds in his own characteristic way. The intensity of this conflict also tends to spontaneously induce the negative feedback mechanism of repression. Male Ss were thus treated to arouse intense oedipal impulses during an interview following each hypnotic session. Each S was exposed to both a free imagery and a nondirective interview. Ss were concurrently assigned to one of six drug groups and received the same drug treatment during each session. Results indicate that this search for a therapeutic technique, drug, or specific combination of the two that would significantly reduce the time necessary in psychotherapy for the uncovering and resolution of repressed, intrapsychic conflict was unsuccessful. Use of the free imagery psychotherapy technique and low dosages of amphetamine, however, significantly increased the level of expressed affect, but this affect was not appropriately integrated within the time span of two therapy hours. (Journal abstract modified)

222725 Waddell, Kathleen Jo. University of Montana **The effects of methylphenidate hydrochloride on psycholinguistic, motor and visual-perceptual abilities of hyperkinetic children with learning disabilities. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 75-12603 HC$13.50 MF$5.00 94 p.

Thirty hyperkinetic children with learning disabilities were administered methylphenidate (Ritalin), placebo and no drug treatments in a triple blind repeated measures design. Five hyperkinetic children with learning disabilities served as a control. The results indicate that methylphenidate clearly improves verbal expression and visual association abilities. Significant treatment X order effects are reported in the visual receptive and visual closure and visual association areas. The most potent treatment effects occurred when methylphenidate was administered last in the order sequence. This finding suggests that methylphenidate enhances performance, and is most effective after a child has become familiar with a task. (Journal abstract modified)

222871 Bowen, Florry P.; Kamienny, Robin S.; Burns, Margaret M.; Yhar, Melvin D. Department of Neurology, Mount Sinai School of Medicine, Fifth Avenue and 100th St., New

York, NY 10029 **Parkinsonism: effects of levodopa treatment on concept formation.** Neurology. 25(8):701-704, 1975.

Concept formation was compared in 71 parkinsonian patients and 35 controls matched for age and scores on the verbal portion of the Wechsler Adult Intelligence Scale. It was found that the patients formed significantly fewer concepts, as measured by the Wisconsin Card Sorting Test (WCST). The patients had difficulties in shifting sets and were unable to attend to the completion of a concept. Levodopa treated patients were able to produce more correct responses, but were still unable to maintain the correct responses to produce more correct concepts than nonlevodopa treated patients. The behavior of the parkinsonian patients on the WSCT is similar to that of patients who have undergone frontal lobectomy. The results indicate that levodopa therapy may improve vigilance without increasing the patient's overall cognitive ability. 33 references. (Author abstract)

223394 Weckowicz, Thaddeus E.; Fedora, Orest; Mason, John; Radstaak, Donald; Bay, Kyung S.; Yonge, Keith A. Department of Psychiatry, University of Alberta, Edmonton, Alberta, Canada **Effect of marijuana on divergent and convergent production cognitive tests.** Journal of Abnormal Psychology. 84(4):386-398, 1975.

The effects of various dosage levels of marihuana on selected psychomotor performance and cognition tests were studied. Subjects were 84 young male volunteers divided into four groups: high and low dose, placebo and control. It was discovered that even the subjects who received the low dose showed impairment on the Wechsler Adult Intelligence Scale Block Design Test and Memory-for-Designs Test. The high dose subjects gave an impaired performance on several other cognitive tests. However, on some cognitive tests, mainly those measuring divergent production and oral fluency, the low dose subjects performed the best and the high dose subjects performed the worst. Consequently there is a possibility, requiring further exploration, that cannabis at low dose levels can act as a stimulant and can improve performance on certain tests. Results of some 15 earlier published studies on the effects of cannabis are summarized in tabular form. 72 references. (Author abstract modified)

224193 Tsutsui, Sueharu; Saito, Toshiji; Tsushima, Munenori. Second Department of Internal Medicine, Toho University School of Medicine, Japan **Clinical trial of oxypertine in the treatment of psychosomatic disorders, neurosis and depression.** Medical Consultation & New Remedies (Tokyo). 11(10):2065-2070, 1974.

The effect of oxypertine on psychosomatic disorders, neuroses and depression was studied, based on an experiment in which eight patients with psychosomatic diseases, five with neuroses and seven with depression were treated with this drug (10-30mg/day) for 3-120 days. Oxypertine was effective in 65% of the patients; it was most effective in those patients with psychosomatic disorders and least effective in neurotics. Positive effects were noted in treatment of a stiff shoulder, general fatigue, nausea, loss of appetite, insomnia, depressive feeling, and lack of volition. Side-effects included general fatigue, tachycardia, dizziness and an abnormal sensation of the face; no correlation was observed between onset of side-effects and drug dosage. 4 references.

224195 Kimura, Sada; Kanno, Takanori. Department of Neuropsychiatry, Kansai Medical University, Japan **Clinical experience of the use of FK-880 (sulpiride) for depression and neurosis.** Medical Consultation & New Remedies (Tokyo). 11(12):2591-2601, 1974.

The effects of sulpiride (FK-880) on 24 depressed and 9 neurotic patients are reported. Ss were administered 150-300mg/day of sulpiride for 10-206 days. Treatment was effective overall in two thirds of all patients, but was more effective in nonmelancholic than in melancholic depressives. Improvement appeared within 7 days and the most effective dosage was 300mg/day. Minor side-effects, including one case of akathesia and one case of edema, were observed. 17 references.

224379 Safer, Daniel J.; Allen, Richard P. Division of Child Psychiatry, Johns Hopkins University School of Medicine, 601 N. Broadway, Baltimore, MD 21205 **Stimulant drug treatment of hyperactive adolescents.** Diseases of the Nervous System. 36(8):454-457, 1975.

The characteristics and classroom behavior changes of hyperactive (HA) schoolchildren treated with stimulants during the years 1969-1974, were evaluated in relation to the age of the child. The major findings were as follows: 1) the therapeutic response to stimulants for hyperactivity did not significantly change from age 6 to age 16; 2) pretreatment teacher ratings indicated that as a group, teenage HA children were as inattentive as younger HA children but less aggressive and overactive; 3) the mean dose of stimulant medication to achieve a successful classroom response for school age HA children did not significantly increase with age; 4) parental resistances to stimulants were not related to the age of the HA child, but behavioral resistances by the child increased significantly during the teens. There were no reports of abuse of stimulants by HA teenagers. 26 references. (Author abstract modified)

224753 Mendelson, Jack H.; Mello, Nancy K. Alcohol and Drug Abuse Research Center, Harvard Medical School, McLean Hospital, Belmont, MA **Alcohol and marijuana: comparative psychopharmacology.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 71-72).

At the 128th Annual Meeting of the American Psychiatric Association, held at Anaheim, California, May 1975, a paper was presented which reported on comparative psychopharmacology for alcohol and marihuana effects on human behavior, as studied in over 100 male alcohol addicts and in 50 male marihuana users. Findings indicate that alcoholics did not function well in the work environment and did not work during periods of heavy drinking, while marihuana abusers worked at very high rates even when smoking, although they showed a dose related decrement in operant work on the day following heavy intake. Findings suggest that both alcohol and marihuana adversely influence motivation to work. Both alcoholics and marihuana smokers developed dysphoric mood states as drug use progressed, while the former became hostile and aggressive more often than the latter Ss. Serial determinations of plasma testosterone levels decreased in alcohol addicts during consumption, but this did not occur with marihuana users. Finally, it was noted that the relationship between variations in plasma testosterone levels and sexual and aggressive behavior remain to be determined. (Journal abstract modified)

224754 Salzman, Carl; van der Kolk, Bessel; Shader, Richard I. Massachusetts Mental Health Center, Boston, MA **Marijuana and hostility in a small group setting.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 72-73).

At the 128th Annual Meeting of the American Psychiatric Association, Anaheim, California, May 1975, a paper was presented which reported the incidence of hostility in a small group setting where Ss either smoked marihuana or received a placebo. Data suggest that marihuana use in such a setting decreases inner feelings of hostility and anger, although it does not necessarily decrease verbal hostile behavior, since sarcasm was shown to increase. Following a frustration stimulus, however, both inner feelings of hostility and outer directed hostile behavior decreased, resulting in an increased sense of cohensiveness among the group and improved task oriented behavior. Findings confirm the previous pilot results and further suggest that marihuana contributes to an improvement in group cohesion and task performance following frustration. (Journal abstract modified)

224755 Melges, Frederick T. Department of Psychiatry, Stanford University Medical Center, Palo Alto, CA 94305 **Marijuana, alcohol and interpersonal perceptions.** In: Scientific proceeedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 73-74).

At the 128th Annual Meeting of the American Psychiatric Association, Anaheim, California, May 1975, a paper was presented which described the relationships between alcohol and marihuana induced changes in temporal organization and interpersonal perceptions. The same Ss were compared during tetrahydrocannabinol (THC) and alcohol intoxication, and interpersonal perception scales showed significant differences between the two states. Compared to alcohol, marihuana induced greater changes in time sense, increased concentration on the present and a prolongation of subject duration at low to moderate doses. Ss' perception of time was thus childlike with associated euphoria and freshness and heightening of perception. Higher doses, however, induced a fragmentation of personal time and consequent mistiming of interpersonal transactions. This was associated with disjunctive self - other perceptions and may have given rise to feelings of suspiciousness, depersonalization, and isolation in contrast to comparable doses of alcohol. It was noted that, in examining the social use and abuse of these drugs, it is important to distinguish between their recreational and isolation effects, since these appear to be dose dependent. (Journal abstract modified)

224756 Weingartner, Herbert; Stillman, Richard. Adult Psychiatry Branch, NIMH, Bethesda, MD **Experiencing and altering states of intoxication: an information processing view of the high.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (P. 74-75).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, May 1975, a paper was presented which reported the effects of alcohol and marihuana intoxication on information processing. An overview of recent research indicated that: (1) much of the learning stored while intoxicated was more effectively retrieved when Ss were again drugged than when in the undrugged state; (2) information which was difficult to code was particularly susceptible to dissociation in crossing states, learning in one state and recalling in some disparate state; (3) what appeared to be lost in recall when learning occurred while intoxicated or where retrieval was attempted undrugged (or vice versa) were clusters or higher order memory units, rather than the fine detail of previously stored experience; (4) information which could not be recalled in some disparate retrieval state was often available in memory, but inaccessible; and (5) the intoxicated states could be effectively viewed in terms of systematic and intrasubject consistent alterations in the strategies by which experiences and information were transfromed and stored in input, and the related retrieval strategies that were state specific and necessary for later recall of these experiences. (Journal abstract modified)

224757 Galanter, Marc. Department of Psychiatry, Albert Einstein College of Medicine, Bronx, NY **The intoxication: state of consciousness.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 75-76).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, May 1975, a paper was presented which advanced the hypothesis that the totality of altered psychophysiological responses effected by marihuana intoxication engenders an intoxication state of consciousness. A model of drug seeking behavior was developed to integrate three categories of experimental data: 1) changes in external perception which have electroencephalogram analogues; 2) the subjective experience of intoxication which points to a complex interaction among subject, drug and subculture and which is perceived as internal experience; and 3) the state-dependent nature of cognition in which intoxication summons a different network of cognitive capacities as a result of state-dependent recall. The heuristic value of defining an intoxication state of consciousness with regard to the understanding of certain clinical aspects of drug abuse and its treatment was also discussed. (Journal abstract modified)

224796 Post, Robert M.; Kopanda, Richard T. 3-West Clinical Research Unit, Section on Psychobiology, Adult Psychiatry Branch, NIMH, Bethesda, MD 20014 **Cocaine, kindling, and psychosis.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 129-130).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, a paper was presented suggesting that the progressive effects of cocaine in animals and man may be related to the phenomenon of kindling in which repetitive, intermittent electrical stimulation of the limbic system (particularly the amygdala) produces increasing excitatory effects and, ultimately, convulsions. Once an animal is kindled, a previously subconvulsive electrical stimulation will consistently evoke seizures, even as long as 6 months after the kindling. A relatively permanent functional neural reorganization apparently occurs in the limbic system. Cocaine produces marked spindling, afterdischarges, and seizures in limbic structures. Its capacity for inducing euphoric/dysphoric effects and eventually paranoid psychosis in man may thus be mediated by limbic aminergic mechanisms. Alterations in the limbic system have also been closely linked to pathological behavior in animals and psychotic behavior in man. The cocaine model for psychotic syndromes suggested herein integrates both pharmacological and neurophysiological mechanisms in the progressive and striking alterations in behavior observed with chronic cocaine administration in animals and men. (Journal abstract modified)

224797 Ellinwood, Everett H., Jr. Department of Psychiatry, Duke University Medical Center, Durham, NC 27706 **Prepotent behaviors in amphetamine model psychosis.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 130-131).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, a paper was presented comparing analogous development of disordered behaviors in humans (amphetamine psychosis). Animal experiments were reviewed which demonstrate that the topography and development of behavior disorders, especially stereotypes associated with chronic amphetamine intoxication, reflect learned behaviors, species specific behaviors, behaviors associated with amphetamine arousal, and novel behaviors reflecting unique experimental circumstances prevailing at the time of the initial dose of amphetamine. Evidence relating the amphetamine stimulation of catecholamine systems, that appear to not only mediate many aspects of reinforcement but also subserve many species specific behaviors, was also reviewed. Clinical reports suggesting that similar species specific behaviors are induced in humans with chronic amphetamine intoxication were also summarized. Finally, evidence that the dyskinesias and parakinesias result from supersensitive catecholamine systems was presented. (Journal abstract modified)

225065 Angrist, Burton M.; Sathananthan, Gregory; Thompson, Hyacinth; Gershon, Samuel. Neuropsychopharmacology Research Unit, Dept. of Psychiatry, NYU Medical Center, 550 1st Ave., New York, NY 10016 **A clinical trial of a structurally unique neuroleptic (SU-23397).** Current Therapeutic Research. 18(2):359-363, 1975.

An open dose tolerance and early efficacy study of SU-23397 in 10 schizophrenics and one manic patient is reported. Subjects showed a good tolerance to dosages up to 300mg/day. The structurally unique neuroleptic proved both to be therapeutically efficacious and to cause extrapyramidal side-effects. 1 reference. (Author abstract modified)

225382 Beck, Leah; Langford, William S.; MacKay, Mary; Sum, Grace. Columbia University College of Physicians and Surgeons, 722 West 168th St., New York, NY 10032 **Childhood chemotherapy and later drug abuse and growth curve: a follow-up study of 30 adolescents.** American Journal of Psychiatry. 132(4):436-438, 1975.

Correlation of methylphenidate medication in childhood with later drug abuse and growth in height was studied. Thirty adolescents with histories of minimal brain dysfunctions who had been treated for at least six months with chemotherapy were compared with 30 adolescents who had not been so treated. The findings do not indicate that methylphenidate prescribed in childhood contributes to later drug abuse or seriously interferes with growth in height. 5 references. (Journal abstract modified)

225455 Ayllon, Teodoro; Layman, Dale; Kandel, Henry J. Georgia State University, University Plaza, Atlanta, GA 30303 **A behavioral-educational alternative to drug control of hyperactive children.** Journal of Applied Behavioral Analysis. 8(2):137-146, 1975.

A behavioral procedure for controlling hyperactivity without inhibiting academic performance is described. By means of a time sample observational method, the hyperactivity displayed by three schoolchildren was recorded during math and reading classes. Concurrently, math and reading performances were measured. The study consisted of two baselines, one while the children were on medication and the second while they were off medication. A multiple baseline design across the two academic subject matters was used to assess the behavioral intervention, which consisted of token reinforcement for correct academic responses in math and subsequently math and reading. Discontinuation of medication resulted in a gross increase in hyperactivity from 20% to about 80%, and a slight increase in math and reading performance. Introduction of a behavioral program for academic performance, with no medication, controlled the children's hyperactivity as effectively as when they were on drugs (about 20%). At the same time, math and reading performance for the group jumped from about 12% during baseline to a level of over 85% correct. Each child performed behaviorally and academically in an optimal manner without medication. 27 references. (Journal abstract modified)

225486 Halbreich, U. Rehovoth P. O. B. 1, Israel **Tegretol dependency and diversion of the sense of taste.** Israel Annals of Psychiatry and Related Disciplines (Jerusalem). 12(4):328-332, 1974.

A case history is presented of an alcoholic patient who exchanged addiction to alcohol for a dependence on tegretol. It was found that the drug influenced his sense of taste to such a degree that the individual was unable to drink alcohol. It is indicated this phenomena lasts as long as the individual takes the drug, even continuing some months after the drug is no longer taken. Addiction to Tegretol is explained by several of its mental and neurological side-effects. It is concluded that the sense of taste is influenced by the drugs pharmacological action on the central nervous system. 15 references. (Author abstract modified)

225520 Adams, Perrie M.; Barratt, Ernest S. Dept. of Psychiatry, Univ. of Texas Medical Branch, Galveston, TX **Effect of chronic marijuana administration on stages of primate sleep-wakefulness.** Biological Psychiatry. 10(3):315-322, 1975.

The effects of the repeated administration of delta9-tetrahydrocannabinol on sleep/wakefulness patterns were studied in adult male squirrel monkeys. The percent time spent in slow wave sleep was reduced with chronic treatment and failed to return to baseline levels after 30 days of recovery. The amount of time spent in stage 1 or drowsy state increased with repeated treatment and remained elevated through recovery. Changes observed in other stages of sleep/wakefulness were sensitive to repeated treatment with marijuana but were found to return to baseline levels during recovery. It is concluded that deprivation of a selected stage of sleep over an extended time period similar to that involved with chronic marijuana use may be correlated with changes in lifestyle and efficiency of behavioral responses. 19 references. (Author abstract modified)

15 TOXICOLOGY AND SIDE EFFECTS

213522 Shopsin, Baron; Hirsch, Jacob; Gershon, Samuel. Department of Psychiatry, New York University Medical Center, New York, NY **Visual hallucinations and propranolol.** Biological Psychiatry. 10(1):105-107, 1975.

In order to evaluate the antipsychotic effects of propranolol administration in acute hospitalized schizophrenics, 40mg of propranolol was given to one patient in an oral dose. The patient reported visual hallucinations at the time of maximal beta blockade as indicated by reduction in blood pressure (BP). The fourth patient showed no change in clinical psychopathology and no significant pulse/BP reduction consequent to propranolol ingestion. There is no evidence to indicate that there is an important incidence of visual hallucinations associated with propranolol treatment. 7 references.

213532 Varga, Ervin; Haher, E. Janet;Simpson, George M. Research Center, Rockland State Hospital, Orangeburg, NY **Neuroleptic-induced Kluver-Bucy syndrome.** Biological Psychiatry. 10(1):65-68, 1975.

Two cases of transient, episodic Kluver-Bucy like syndrome are reported. These reactions occurred on various neuroleptics and were not controlled by increasing the dosage of neuroleptics. The episodes were transient and highly dramatic (they were thought to be hysterical at first but were unresponsive to a placebo injection). Their onset was acute, and the symptoms could be controlled with antiparkinson agents. 10 references. (Author abstract)

213706 Lipton, Morris A. Child Development Research Institute, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **/Comment on Linus Pauling's theory of orthomolecular psychiatry./** Comment. American Journal of Psychiatry. 131(11):1266-1267, 1974.

The use of megavitamin therapy in orthomolecular psychiatry is discussed. It is suggested that it is scientifically and economically improper to give huge doses of vitamins when there is no evidence that there is a deficiency in function of any of the enzymes for which they serve as coenzymes. The problem of toxicity is also raised. In extraordinarily large doses, water soluble vitamins have pharmacological effects unrelated to their actions as vitamins and also other metabolic consequences. 10 references.

213708 Heiser, Jon F.; Wilbert, Donald E. Department of Psychiatry and Human Behavior, California College of Medicine, University of California Irvine, CA **Reversal of delirium induced by tricyclic antidepressant drugs with physostigmine.** American Journal of Psychiatry. 131(11):1275-1277, 1974.

The reversal of delirium induced by tricyclic antidepressant drugs with physostigmine is reported. It was found that 2mg of physostigmine given intramuscularly was effective in reversing acute brain syndromes in two patients who had ingested toxic doses of drugs with anticholinergic properties (amitriptyline alone and an amitriptyline - perphenazine combination). Physostigmine also controlled one patient's tachycardia and tachypnea. Physostigmine may not control toxic effects of anticholinergic drugs when these effects are not mediated through cholinergic blockade. 21 references. (Journal abstract modified)

213710 Knee, Steven T.; Razani, Javad. Psychiatric Outpatient Dept., Los Angeles County-Univ. of Southern California Medical Center, 1237 Mission Rd., Los Angeles, CA 90033 **Acute organic brain syndrome: a complication of disulfiram therapy.** American Journal of Psychiatry. 131(11):1281-1282, 1974.

Consecutive admissions over a 3 month period to a general psychiatric ward in a large urban medical center were reviewed for the presence of acute organic brain syndrome in patients being treated with disulfiram for chronic alcoholism. Five such cases were identified. The patients had initially been misdiagnosed as schizophrenic and had been treated with psychotropic medications, generally with less than optimum results. The withdrawal of the offending agent and the use of supportive measures and sedation are suggested, rather than major psychotropic medication as the treatments of choice for this syndrome. 6 references. (Journal abstract modified)

213783 Raj, M. V. Jeeva; Benson, R. Regional Cardiac Unit, Papworth Hospital, Cambridge CB3 8RE, England **Phenothizaines and the electrocardiogram.** Postgraduate Medical Journal (Oxford). 51(592):65-68, 1975.

It is reported that 59 of 140 schizophrenic patients taking phenothiazines were found to have abnormal electrocardiograms (ECG). The abnormalities included T-wave changes, S-T depression, P-R and Q-T prolongation, persistent sinus tachycardia and right bundle branch block. In 48 of the 59 patients, the ECG abnormalities disappeared after stopping the phenothiazine and reappeared on its resumption. 8 references. (Author abstract)

214010 Gerlach, J.; Thorsen, K.; Fog, R. Sct. Hans Hospital, Dept. E, DK-4000 Roskilde, Denmark **Extrapyramidal reactions and amine metabolites in cerebrospinal fluid during haloperidol and clozapine treatment of schizophrenic patients.** Psychopharmacologia (Berlin). 40(4):341-350, 1975.

Eight male schizophrenic patients participated in a double0blind, cross over study of the extrapyramidal side-effects of haloperidol and clozapine (acute dystonia, Parkinsonism and tardive dyskinesia), together with their effect on homovanillic acid (HVA) and 5-hydroxyindoleacetic acid (5-HIAA) in the cerebrospinal fluid (CSF). Haloperidol (9mg/day) caused Parkinsonism, reduce tardive dyskinesias and increased the HVA concentration in the CSF. Clozepine (225 mg/day) had no effect on the neurological phenomena but reduced HVA and 5-HIAA concentrations in the CSF. During the discontinuation phase following the administration of haloperidol, tardive dyskinesia occurred or was aggravated; this did not occur after administration of clozapine. Accordingly, it is suggested that clozapine does not induce dopaminergic hypersensibility and, therefore, will not induce tardive dyskinesias. 36 references. (Author abstract)

214834 Capstick, N. Graylingwell Hospital, Chichester, Sussex, England **Depressive reactions in the course of clomipramine therapy used in the treatment of obsessional conditions.** Scottish Medical Journal (Glasgow). 20(Suppl. 1):45-48, 1975.

In a small series of patients suffering from obsessional disorders, the same type of depression was found which occurs during the course of clomipramine therapy. It is hypothesized that the depression may be secondary to agitation and tension which are recognized side-effects of clomipramine. The patients nevertheless showed improvement in their obsessional symptomatology. Clomipramine seems to have an antiobsessional effect which is distinct from its antidepressant property. 3 references. (Author abstract modified)

215151 Wynne-Hughes, I. Llandudno, Wales **On-going studies of clomipramine (Anafranil) in general practice.** Journal of International Medical Research (Cambridge). 3(Suppl.1):55-62, 1975.

Ongoing studies of clomipramine (Anafranil) therapy are described. Particular attention is being given to dosage regimes, methods of patient self-assessment, sexual side-effects, and weight gain. 14 references. (Author abstract)

215153 Beaumont, G. Geigy Pharmaceuticals, Macclesfield, Cheshire, England **Some practical considerations in the use of clomipramine (Anafranil) in general practice.** Journal of International Medical Research (Cambridge). 3(Suppl.1):72-78, 1975.

The expectation of success in treating depression with clomipramine (Anafranil) in general practice is discussed with a recommendation to adopt a flexible approach to dosage.

Some side-effects are discussed and the differentiation between unwanted pharmacological effects and true toxic effects is stressed. Contraindications both absolute and relative are considered. The importance of possible drug interaction is emphasized. 53 references. (Author abstract)

215670 Aronow, Wilbert S.; Cassidy, John. Cardiology Section, Medical Service, Long Beach VA Hospital, Long Beach, CA 90801 **Effect of smoking marihuana and of a high-nicotine cigarette on angina pectoris.** C;inical Pharmacology and Therapeutics. 17(5):549-554, 1975.

The effects of smoking marihuana and of high nicotine cigarettes on exercise induced angina pectoris were examined. Smoking one marihuana cigarette increased the resting product of systolic blood pressure times heartrate 54%, increased the venous carboxyhemoglobin level, and decreased the exercise time until angina 50% in 10 patients with angina pectoris. Smoking one high nicotine cigarette increased the resting product of systolic blood pressure times heartrate 36%, increased the venous carboxyhemoglobin level, and decreased the exercise time until angina 23%. Smoking either marihuana or high nicotine sigarettes decreases exercise performance until angina by increasing myocardial oxygen demand and by decreasing myocardial oxygen delivery. Smoking one marihuana cigarette decreased the exercise time until angina more than smoking one high-nicotine cigarette. 9 references. (Author abstract)

215681 Orlandi, F.; Bamonti, F.; Dini, M.; Koch, M.; Jezequel, A. M. School of Medicine, University of Ancona, Ancona, Italy **Hepatic cholesterol synthesis in man: effect of diazepam and other drugs.** European Journal of Clinical Investigation (Berlin). 5(2):139-146, 1975.

The hepatic synthesis of cholesterol, measured as incorporation of 14C-acetate into digitonin precipitable sterols, has been evaluated in needle biopsy material of normal untreated patients and patients under short-term treatment with diazepam, phenobarbital, cholorpromazine or diphenylhydantoin. A significant increase of cholesterol synthesis was observed in the first two groups with much higher levels of incorporation in the diazepam treated patients. Moreover, in this group the levels were still elevated from 4 to 7 days after drug withdrawal. Ultrastructural and morphometric studies performed on the same biopsy material showed a significant increase of smooth endoplasmic reticulum in hepatocytes of diazepam treated patients; in addition, there seemed to be a positive correlation between the increased cholesterol synthesis and the formation of areas of nonvesicular, type 2, smooth endoplasmic reticulum. These findings suggest an early stimulation of the liver cell microsomal system by diazepam in man. They also point to side-effects of some drugs which are not predictable from studies in Wistar rats. 43 references. (Author abstract)

216184 Ban, Thomas A. Department of Psychiatry, McGill University, Montreal, Canada **Drug interactions with psychoactive drugs.** Diseases of the Nervous System. 36(4):164-166, 1975.

Drug interactions, commonly defined as modifications of the action of a drug by another exogenous chemical, is discussed in regard to the prescription of psychoactive drugs. Four mechanisms involved with drug interactions with psychoactive drugs are identified and discussed. These include, the alteration of absorption, modification of action at receptor sites, modification of biotransformation, and alteration of excretion. It is suggested that the combined administration of psychoactive medication and specific drugs for the particular disorder is dependent on the developmental stage of the disease. It is concluded that acceptance of this theoretical framework would vastly extend the area of medical practice in which drug interactions with psychoactive drugs may occur. 20 references.

216391 Tamazawa, Akira; Ichinowatari, Naomichi; Nakajima, Setsuo; Aida, Nobuo; Kano, Rikihachiro. Department of Internal Medicine, Sakuraga-oka Sanatorium, Japan **Report on three cases of cardiac changes during treatment with floropipamide (Propitan).** Clinical Psychiatry (Tokyo). 17(1):51-57, 1975.

Three cases of electrocardiogram (EKG) abnormalities observed during treatment with floropipamide (Propitan) are discussed. Ss included a 30-year-old psychotic male, a 40-year-old male schizophrenic, and a 46-year-old male alcoholic who had been treated with various psychotropic drugs. EKG abnormalities observed included elongation of the QT-complex and a change in the T-wave immediately after treatment with 900mg of Propitan. The changes immediately disappeared after termination of drug treatment, and in one case the same abnormalities were later reinduced by treatment with the same drug. It is concluded that large doses of butyrophenone derivatives should be prescribed carefully. 18 references.

216766 Vauterin, C.; Veillon, F. Hopital du Val-de-Grace, 75230 Paris Cedex 05, France **/A clinical study of a new neuroleptic extrapyramidal syndrome corrector with acute psychotic states./** Etude clinique d'un nouveau correcteur du syndrome d'impregnation neuroleptique dans les etats psychotiques aigus. Encephale (Paris). 1(1):61-68, 1975.

At the Ninth Congress of the International College of Neuro-psychopharmacology, Paris, July 1974, a paper was presented in which research on the corrective action of tropatepine hydrochloride on the extrapyramidal effects caused by neuroleptic drugs was reported. Satisfactory results were obtained with daily doses of 10-20mg in 30 cases. The drug's effect on dyskinetic crises was particularly good and fast. The akinetic, hypertonic syndrome was efficiently corrected in 18 cases out of 23. The hyperkinetic manifestations (akathisia, taxikinesia) reacted favorably in 8 cases out of 11, dysarthria in 7 cases out of 11. The decrease in tremor, dryness of mouth, and visual accommodation disorders were less satisfying. Clinical tolerance was excellent. With the doses used, there was no atropinic effect, vigilance disorder, drug dependence. Daily administration of a 10mg tablet was sufficient in 19 cases. 13 references. (Author abstract modified)

216767 Caroli, F.; Littre-Poirier, M.-F.; Ginestet, D.; Deniker, P. Service hospitalo-universitaire de Sante mentale et de Therapeutique, Hopital Sainte-Anne, 75674 Paris Cedex 14, France **/Trial interruption of antiparkinsonians in long-term neuroleptic treatment./** Essai d'interruption des antiparkinsoniens dans les traitements neuroleptiques au long cours. Encephale (Paris). 1(1):69-74, 1975.

At the Ninth Congress of the International College of Neuro-psychopharmacology, a paper was presented in which results were reported of an attempt to interrupt antiparkinsonian treatment in chronic psychotic patients who had been treated with neuroleptics for at least three months. After three weeks, 72% of the patients had to receive the earlier corrective treatment because of the reappearance of extrapyramidal manifestations: half of the Ss took the antiparkinsonian during the first week and more than a third presented an acute psychotic attack when the antiparkinsonian medication was discontinued. After three weeks, 28% of the total sample were still on placebo. The psychotropic activity of an-

tiparkinsonian medications, the effect of neuroleptic doses, and the characteristics of each neuroleptic used are discussed. It is concluded that the administration of antiparkinsonians continuously is necessary in most cases during prolonged treatment of chronic psychotics. 3 references. (Journal abstract modified)

216965 Blomgren, Barbara; Huey, Leighton. Dept. of Psychiatry, Unv. of California at San Diego, School of Medicine, LaJolla, CA 92037 **Amphetamine psychosis or paranoid schizophrenia?** Western Journal of Medicine. 122(5):394-405, 1975.

Amphetamine psychosis mimicking paranoid schizophrenia is discussed, based on a case presentation by Dr. Heywood Zeidman and a patient interview conducted by Dr. Morris Oscherwitz. A discussion by Dr. Oscherwitz and Dr. Dominick Addario centers on three basic questions: 1) whether or not amphetamines precipitate schizophrenia; 2) neurochemical pathways, physiological mechanisms and personality features that schizophrenics and amphetamine users have in common; 3) whether or not certain persons more susceptible than others to amphetamine psychosis. The widespread use of amphetamines is pointed out. No relationship is seen between the incidence of amphetamine psychosis and the duration or amount of drug use. Differences between amphetamine psychosis and schizophrenia are outlined. It is believed that amphetamines acting at dopamine and norepinephrine neurons may account for amphetamine psychosis. It is concluded that the case is a schizophreniform psychosis due to amphetamines in a person with a premorbid schizoid makeup. The importance of developmental history is stressed. It is suggested that people who choose amphetamines may be fixated in the separation - individuation conflict. 13 references.

217453 Floru, L.; Tegler, J.; Wilmsen, H. Psychiatrischen Universitatsklinik, Rheinisches Landeskrankenhaus, Bergische 2, D-4 Dusseldorf 12, Germany **/Studies of lithium induced tremor by means of different measurement methods./** Untersuchungen de lithiumbedingten Tremors mit verschiedenen Messmethoden. International Pharmacopsychiatry (Basel). 10(2):100-110, 1975.

The character of lithium induced tremor is discussed. Three various measuring methods are presented: an accelerometer, a hole plate and an apparatus based on aimed tapping. A fourth apparatus is proposed. The first three methods were applied on 16 patients who received lithium therapy and on a control group consisting of 22 normal persons. The results were statistically evaluated. For registering the postural component of lithium induced tremor, the first two methods proved themselves worthy of recommendation in quotidian practice. Frequency and amplitude of lithium induced tremor till the ninth day of drug administration are discussed. 15 references. (Author abstract)

217668 Stafford, Calvin R.; Bogdanoff, Bruce M.; Green, Lawrence; Spector, Harvey B. Department of Neurology, Crozer-Chester Medical Center, 15th St. and Upland Ave., Chester, PA 19013 **Mononeuropathy multiplex as a complication of amphetamine angiitis.** Neurology. 25(6):570-572, 1975.

A patient who abused multiple drugs and developed a rapidly progressive mononeuropathy multiplex, which appeared to respond to corticosteroid therapy with partial resolution was examined. Intravenous methamphetamine had been used almost exclusively from the fourth month prior to the onset of symptoms. Biopsy material revealed a necrotizing angiitis involving medium and small sized arteries, capillaries, and venules, typical of a hypersentitivity type angiopathy, rather than the previously reported polyarteritis nodosa type lesions secondary to illicit drugs. The apparent response to corticosteroids suggests that these agents might be useful in the treatment of some complications of drug abuse. 8 references. (Author abstract)

217969 Gupta, R. K.; Montgomery, Stuart. M.R.C. Neuropsychiatry Laboratory, West Park Hospital, Epsom, Surrey, England **Status of lithium patients as blood-donors.** Lancet (London). 1(7911):860, 1975.

Problems encountered by patients treated with lithium carbonate when they volunteered to donate blood are discussed. It is noted that lithium is fairly evenly distributed in the body water both intracellularly and extracellularly and is assumed that it should be diluted in the recipient's body water. The resultant dilution would reduce the lithium concentration to levels which are of no biological significance. Permission is advocated for lithium treated patients to donate blood. 4 references.

218155 Shader, Richard I.; Greenblatt, David J.; Salzman, Carl; Kochansky, Gerald E.; Harmatz, Jerold S. Massachusetts Mental Health Center, 74 Fenwood Road, Boston, MA 02115 **Benzodiazepines: safety and toxicity.** Diseases of the Nervous System. 36(5, Section2):23-26, 1975.

Clinical studies of the toxicity and side-effects of benzodiazepines are reviewed. Investigations indicate that these agents have a low frequency of side-effects and of clinically significant drug interactions at therapeutic dosage levels, and exhibit a wide margin of safety before habituation and physiological dependence occur. 20 references. (Author abstract modified)

218557 Beumont, P.; Bruwer, J.; Pimstone, B.; Vinik, A.; Utian, W. Dept. of Psychiatry, Groote Schuur Hospital, Observatory, Cape, South Africa **Brom-ergocryptine in the treatment of phenothiazine-induced galactorrhoea.** British Journal of Psychiatry (London). 126:285-288, 1975.

The effects of an ergot alkaloid, 2-bromo-alpha-ergocryptine (bromergocryptine) on the raised prolactin levels, galactorrhea and menstrual disturbances that arise in patients as a result of psychotropic medication were investigated. Nine female patients at a psychiatric hospital, aged 27 to 49, participated. In none of the Ss did the galactorrhea completely disappear during the course of treatment, but in all five instances in which it was pronounced there was a marked decrease in the amount of the secretion. Only one S had a change in menstrual functioning. There was a marked variation in mean prolactin values for individual Ss for the different weeks of the investigation, irrespective of whether bromergocryptine was being administered. Findings agree with the suggestions that bromergocryptine acts mainly at the level of the pituitary prolactin producing cells. 8 references.

218773 Rifkin, Arthur; Quitkin, Frederic; Klein, Donald F. Long Island Jewish-Hillside Medical Center, Hillside Division, Glen Oaks, NY 11004 **Akinesia: a poorly recognized drug-induced extrapyramidal behavioral disorder.** Archives of General Psychiatry. 32(5):672-674, 1975.

Eight case histories of patients who, after reaching clinical stability while receiving a constant dose of antipsychotic medication and procyclidine hydrochloride, participated in a procyclidine withdrawal study are presented to illustrate the seriousness of akinesia as a toxic extrapyramidal side-effect of an-

tipsychotic drugs. The difficulties of differential diagnosis of akinesia is emphasized and the importance of further research in this area is stressed. 6 references. (Author abstract modified)

219353 Lutz, Elmar G. Dept. of Neuropsychiatry, St. Mary's Hospital, Passaic, NJ **Lithium toxicity precipitated by diuretics.** Journal of the Medical Society of New Jersey. 72(5):439-440, 1975.

A confusional state, with disorientation and indistinct speech, occurred in a 53-year-old woman on lithium carbonate maintenance treatment for manic-depressive illness, following the administration of 25 mgs each of the diuretics, spironactolone and hydrochlorothiazide for 19 days. The clinically manifest toxicity subsided rapidly with 1.5days following the decrease of the dosages of both lithium and of hydrochlorothiazide. The acute toxic effect is explained on the basis of acute dilutional hyponatremia as the result of low salt diet plus excessive water intake and intensive diuretic therapy. Close medical supervision is viewed as necessary if lithium therapy is to be effective and safe. 3 references.

219517 Ramanathan, K. B.; Davidson, C. Cardiac Department, Leeds General Infirmary, Leeds LS1 3EX, England **Cardiac arrhythmia and imipramine therapy.** British Medical Journal (London). No. 5959:661-662, 1975.

A case history is reported of a patient who developed recurrent supraventricular arrhythmias and heart failure during treatment with imipramine. When the impramine treatment was discontinued, all her symptoms were resolved and she had no further evidence of cardiac disease. 12 references.

219621 Snyder, Bruce D. Dept. of Neurology, St. Paul-Ramsey Hospital, St. Paul, MN **Physostigmine -- antidote for anticholinergic poisoning.** Minnesota Medicine. 58(6):456-457, 1975.

Physostigmine, a centrally acting anticholinesterase inhibitor, is reported to be an apparently safe and effective antidote for toxic delirium caused by a variety of commonly used drugs. The effectively antagonized intoxicants include not only the belladonna alkaloids but many psychoactive drugs not commonly thought of as exerting a significant atropinic effect. Experience suggests that physostigmine may be used as a diagnostic therapeutic trial for the patient who presents with a delirium or coma and who is thought to have ingested one of these drugs. (Author abstract modified)

219694 Escande, M.; Gayral, L.; Goldberger, E. Hopital de la Grave, 31052 Toulouse Cedex, France **/Depressions and antidepressants during treatment with long-acting neuroleptic drugs: side-effects and the "emergent metatherapeutic syndrome"./** Depressions et antidepresseurs au cours des traitements par les neuroleptiques a effet prolonge: effets secondaires et "syndrome emergent metatherapeutique". Annales Medico Psychologiques (Paris). 2(5):669-694, 1974.

Depressions due to prolonged treatment with neuroleptic drugs were examined, and the effect of treatment with antidepressants was investigated. Of 165 patients, (schizophrenics, acute delirious psychotics, and chronic delirious psychotics), 42 presented with depression or another indication for the use of an antidepressant. With acute delirious psychoses, the neuroleptic is depressogenic. The appearance of a depression seems to mark the definitive end of the psychotic experience; it is sensitive to tricyclic drugs. With chronic delirium, side-effects of the parkinsonian and inertia - passivity type are frequent. With schizophrenia, the inertia - passivity syndrome is accompanied by more or less atypic and long-lasting depressive tendencies and an emergent metatherapeutic syndrome. The effect of tricyclics is variable. 31 references.

219827 Abdessemed, H.; Gaillard, L.; Gaussel, D. Centre Anti-Poisons, Hopital E.-Herriot, Lyon, France. **/Lithium salt poisoning in an 8-year-old child./** Intoxication par sel de lithium chez un enfant de 8 ans. Bulletin de Medecine Legale et de Toxicologie Medicale (Lyon). 18(2):141-142, 1975.

A case of lithium poisoning in an 8-year-old child is reported, in which clinical examination revealed behavioral disturbances, manifested by delirious attacks and agitation. Results of the boy's neurological examination were normal, as well as those from the general examination. The contrast between the psychic disturbances and the absence of any other abnormality indicated poisoning. When it was found that the mother regularly took lithium, the child was given a simple sedative treatment. Forty eight hours later, the lithium level was down and delirious manifestations had completely disappeared, but the patient presented a state of agitation which took a week to disappear completely. The fact that the poisoning occurred in a child and that it caused sufficiently serious symptoms to necessitate hospitalization indicates the need for caution in the use of lithium in treating children.

221165 Shapiro, Arthur K.; Chassan, Jacob; Morris, Louis A.; Frick, Robert. Payne Whitney Clinic, New York Hospital, Cornell University Medical College, 1300 York Ave., New York, NY 10021 **Placebo-induced side effects.** Journal of Operational Psychiatry. 6(1):43-46, 1974.

Placebo induced side-effects were studied in psychiatric outpatients given two psychological tests as part of a larger investigation of the placebo effect. Results confirm the frequent observation that reported side-effects may be exaggerated by patients when treated with drugs or in drug studies. Appropriate placebo controls are essential to minimize the exaggerated reporting of side-effects. 13 references.

221270 van den Berghe, H. Department of Human Biology, Division of Human Genetics, University of Leuven, Minderbroederstraat, 12, B-3000 Leuven, Belgium **Clastogenic effects of haloperidol in vivo and of haloperidol, droperidol, and pipamperone in vitro: a negative study.** Arzneimittel-Forschung (Aulendorf). 24(1):2055-2058, 1974.

The clastogenicity of haloperidol in vivo, and of haloperidol, droperidol and pipamperone in vitro were investigated. No anomalies were discovered in vivo. In vitro, except for some blurring of the chromosomes in a small minority of metaphases, and for a noticeable inhibition of culture growth, no anomalies, and specifically no chromosome damage, could be demonstrated. 1 reference. (Journal abstract)

221307 Mattke, D. J.; Mombour, W.; Glotzner, F. L. Max-Planck-Institut fur Psychiatrie, D 8000 Munich 40, Kraepelinstr. 10 **/The assessment of neuroleptogenic extrapyramidal syndromes in psychopharmacological research./** Erfassung neuroleptisch bedingter extrapyramidaler Syndrome in einem psychopharmakologische Forschungsprojekt. Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 8(1):36-44, 1975.

Methodological questions of clinical observations and classification of drug induced extrapyramidal symptomatology are discussed. In the experiment, two groups of 20 acute

schizophrenic patients each were examined. The patients were treated for 4 weeks under double-blind conditions with the butyrophenone derivative Haloperidol and with the benzoxazepine derivative Loxapin respectively. The patients were examined by means of the Extrapyramidal Symptom Scale weekly, before, during and after this treatment as well as under subsequent therapy with a long-acting neuroleptic. Extrapyramidal disturbances appearing between these fixed rating times were noted in a checklist. According to a classification proposed by Chien and DiMascio, the symptomatology of extrapyramidal disturbances was divided into permanent neuroleptic manifestations and paroxysmal neurodysleptic manifestations. While Haloperidol caused more distinct symptoms of permanent neuroleptic manifestations, acute neurodysleptic reactions appeared more frequently with Loxapin. 7 references. (Journal abstract modified)

221335 Gerlach, J.; Thorsen, K.; Munkvad, I. Sct. Hans Hospital, Department E, DK-4000 Roskilde, Denmark **Effect of lithium on neuroleptic-induced tardive dyskinesia compared with placebo in a double-blind cross-over trial.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 8(2):51-56, 1975.

The value of lithium sulfate in treating patients with neuroleptic induced tardive dyskinesia was assessed in a double-blind crossover study of 15 hospitalized patients. Lithium induced a slight, but significant, reduction in the tardive dyskinesia. Lithium had a suppressive effect on psychomotor agitation and aggression. The concentrations of homovanillic acid and 5-hydroxyindoleacetic acid were determined in the cerebrospinal fluid of five patients. It is concluded that lithium can be used to advantage in the treatment of moderate tardive dyskinesia, particularly when the movement disturbances are accompanied by psychomotor restlessness. Finally, the effect of lithium on the central aminergic transmitter substances is discussed in relation to existing hypotheses on the pathophysiology of tardive dyskinesia. 24 references. (Journal abstract modified)

221336 Eckmann, F.; Schwalb, H.; Hanika, R. Landeskrankenhaus, 238 Schleswig, Muhlenredder 15 **/Psychotropic agents and pathological ECG changes./** Psychopharmaka und Veranderungen im Elektrokardiogramm. Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 8(2):57-68, 1975.

The results are reported of an epidemiological research program on the possible relationship of the intensity of pathological electrocardiogram (ECG) changes to sex, age, the administration of tricyclic and nontricyclic psychotropic agents with or without the combination of glycosides, the potency of neuroleptics and their chemical structure. No statistical significance could be established between pathological ECG changes and such factors as administration of tricyclic and nontricyclic psychotropics with or without the combination of glycosides, or the potency of neuroleptics and their chemical structure. With greater age, the frequency of ECG changes increases independently of psychotropics. The difficulties of data interpretation are discussed. 24 references. (Journal abstract)

221417 Bjorum, Niels; Hornum, Ib; Mellerup, Erling T.; Plenge, Per K.; Rafaelsen, Ole J. Psychochemistry Institute, Rigshospitalet, 9 Blegdamsvej, DK-2100 Copenhagen, Denmark **Lithium, calcium, and phosphate.** Lancet (London). 1(No. 7918):1243, 1975.

The urinary excretion of calcium and phospate was measured before and after the start of lithium therapy. Data indicate that, during lithium therapy, urinary excretion alone gives far from a true picture of total balance of calcium and phosphate, since most of the excretion of calcium and about 50% of the excretion of phosphate takes place via the feces. A thorough investigation of lithium effects on calcium and phosphate metabolism must therefore encompass both urinary and fecal excretion. Preliminary results from studies in progress indicate that lithium induces retention of both calcium and phosphate.

221515 Purgyi, P.; Hegedic, Z. Psychiatrische Universitatsklinik Basel, CH-7000 Basel, Switzerland **/Three acute cases of diphenylhydantoin intoxication./** Uber drei akute Diphenylhydantoin-Intoxikationen. Schweizer Archiv fur Neurologie, Neurochirurgie und Psychiatrie (Zurich). 114(1):195-199, 1974.

The clinical course of three acute cases of diphenylhydantoin intoxication in two patients was studied. The clinical semiotic was characterized by somatic symptoms such as horizontal nystagmus of the visual field, theta and delta wave irregularities in the electroencephalographic pattern, and by psychic symptoms, in particular "Wieck transient syndrome" characterized by hallucinations. The psychopathological symptoms were found to become intensified by the impact of other substances affecting the brain stem and the limbic system. Complete recovery was achieved in the three cases. 15 references. (Author abstract modified)

221633 Jacobsson, L.; Glitterstam, K.; Palm, U. Psychiatric University Department, Lasarettet, 901 85 Umea, Sweden **Objective assessment of anticholinergic side effects of tricyclic antidepressants a controlled study of imipramine and imipramine-N-oxide.** Nordisk Psykiatrisk Tidsskrift (Hisings Backa). 28(6):451, 1974.

A double-blind cross-over comparison between imipramine and imipramine-N-oxide explored the anticholinergic side-effects on salivation and accommodation. Fifteen healthy male volunteers were given 25 mg. three times daily of each drug for 3 days. Saliva from both parotid glands was collected by suction cups covering the salivary ducts and was led through a drop counter connected to an electronic counter. The accommodation capacity was registered by determining the near point with Jaeger's scale mounted on a slide movable on a graded scale. A significantly lower impairment of salivation after imipramine-N-oxide medication compared to imipramine was observed, while no difference was found regarding accommodation. (Author abstract modified)

221663 Jukes, A. M. CIBA Laboratories, Horsham, Sussex, England **Maprotiline (Ludiomil): side-effects and overdosage.** Journal of International Medical Research (Northampton). 3(Suppl. 2):126-131, 1975.

At the Ludiomil Symposium, Stratford-upon-Avon, England, June 1974, a paper was presented in which the clinical picture of intoxication by maprotiline with and without accompanying drugs was described based on 5 cases of suicide and 13 cases of attempted suicide. Maprotiline is certainly as well tolerated as amitriptyline, imipramine, and clomipramine. Side-effects, with the exception of skin rashes, were either similar or lower than those noted with the other compounds. There is at present one known case of death due to acute intoxication by maprotiline taken alone (3g). A fatal outcome has been observed in four cases of combination intoxication. The maprotiline dose range was 2-10g and the additional drugs were tricyclic antidepressants, sedatives or hypnotics. The known maximal intoxication dose where maprotiline was the only drug taken and full recovery occurred is 5g in the case of

a 58-year-old woman. There is no specific antidote to maprotiline. 2 references. (Author abstract modified)

221988 Mannisto, P. T. no address **Hypothyroidism during lithium treatment: a review of 49 cases.** In: Psychiatria Fennica. Helsinki, Helsinki Univ. Central Hosp., 1974. 408 p. (p. 299-305).

The incidence of hypothyroidism during lithium treatment is reported. Case reports of the treatment given to 49 Ss are analyzed in detail, and 61 additional cases of thyroid disorder are mentioned. The mechanism of action of lithium is described and serum protein bound iodine values and thyrotropin stimulating hormone values in the patients are summarized. It is concluded that hypothyroidism develops in less than 5% of patients treated with lithium salts. Three tables concerning etiology, symptomatology, and some precipitating factors are included. Diagnosis of and the medical treatments for the various side-effects of lithium medication are also considered. 88 references.

221990 Penttila, Antti; Lehti, Heikki, Lonnqvist, Jouko. Department of Forensic Medicine and Psychiatric Clinic, Helsinki University, Helsinki, Finland **Nystagmus and disturbances in psychomotor functions induced by psychotropic drug therapy.** In: Psychiatria Fennica. Helsinki, Helsinki Univ. Central Hosp., 1974. 408 p. (p. 315-326).

One hundred patients treated in a psychiatric hospital were surveyed to study the effects of long-term drug therapy on psychomotor functions. Ss were examined to determine reflexes, coordination, and the presence of tremor in the hands. Phenothiazine, benzodiazepine and tricylcic antidepressants were the drugs most often used as medication. The error scores of the tests increased with the number of drugs used and the relative strength of medication. An interesting and unexpected finding was the nystagmus phenomenon. The present results are consistent with earlier observations that the effects of psychotropic drugs and drug combinations on different clinical performances show great individual variation. Forensic and clinical implications are also discussed. 37 references. (Author abstract modified)

222603 Ballinger, Brian R; Ramsay, Anna C. Drug Monitoring Unit, Royal Dundee Liff Hospital, Liff by Dundee, DD2 5NF, Scotland **Accidents and drug treatment in a psychiatric hospital.** British Journal of Psychiatry (London). 126:462-463, 1975.

A survey of 351 accidents occurring in a 2 year period in a psychiatric hospital showed that 77% of the accidents involved female patients and 48% involved patients with organic psychoses; 236 accidents were falls and 280 occurred in the ward setting. In 277 instancess adequate controls were available. Seventy five per cent of the accident patients had received a psychotropic drug on the day of the accident as opposed to 61% of the controls. The possibility that the side-effects of psychotropic drugs may have contributed to some of these accidents is discussed. 4 references. (Author abstract)

223120 Wellens, Hein J.; Cats, Volkert Manger; Duren, Donald R. University Department of Cardiology, Wilhelmina Gasthuis, Amsterdam, The Netherlands **Symptomatic sinus node abnormalities following lithium carbonate therapy.** American Journal of Medicine. 59(2):285-287, 1975.

Symptomatic sinus node abnormalities which occurred in a 56-year-old woman receiving lithium carbonate are reported. Stimulation studies of the heart revealed that only the sinus node was affected. The abnormalities disappeared completely following cessation of lithium therapy. 10 references. (Author abstract modified)

223777 Wilson, R. G.; Hamilton, J. R.; Boyd, W. D.; Forrest, A. P. M.; Cole, E. N.; Boyns, A. R.; Griffiths, K. Department of Surgery, General Hospital, Nottingham, England **The effect of long term phenothiazine therapy on plasma prolactin.** British Journal of Psychiatry (London). 127:71-74, 1975.

The effect of long-term phenothiazine therapy on circulating levels of plasma prolactin was examined in psychiatric inpatients. Plasma prolactin was estimated in Ss receiving either thioridazine (20-300mg/day) or chlorpromazine (50-200mg/day) or other phenothiazine. A homologous radioimmunoassay was used which depends on an antiserum to human amniotic prolactin. Prolactin levels were significantly increased in these patients compared with control patients, and were dose related. Simultaneous estimation of growth hormone revealed normal levels. 16 references. (Author abstract)

224507 Otsuka, Norio; Koga, Yoshihiko; Saito, Masaharu; Hagita, Kazuhiro; Ito, Hitoshi; Miura, Sadanori. Department of Neuropsychiatry, Keio University School of Medicine, Shinanomachi, Shinjuku-ku, Tokyo **On syndrome malin induced by neuroleptica.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(9):961-973, 1974.

Nine cases of syndrome malin induced by neuroleptic drugs are discussed. All the patients were under 19 years of age and either were mentally retarded or suffered from chronic alcoholism. This syndrome was induced by intramuscular injection of haloperidol, levomepromazine and fluphenazine enanthate. Even a small dose of these neuroleptics induced this syndrome in patients with an unstable state of the autonomic nervous system. 27 references.

224719 Karacan, Ismet; Williams, Robert L.; Comstock, Betsy S.; Comstock, Eric G.; Okawa, Masako. Department of Psychiatry, Baylor College of Medicine, Texas Medical Center, San Antonio, TX **EEG sleep patterns and drug abuse.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 30-31).

At the 128th Annual Meeting of the American Psychiatric Association, held at Anaheim, California, in May 1975, a paper was presented in which the effects of drug abuse on electroencephalogram (EEG) sleep patterns in patients being withdrawn from abusive levels of amobarbital, secobarbital/amobarbital, pentobarbital, phenobarbital, methaqualone and diazepam were reported. Both conventional EEG parameters and the characteristics of spindle and eye movement activity were analyzed. In general, conventional EEG parameters discriminated among drugs much less definitively than spindle and eye movement characteristics. However, at titration and subsequent very high dose levels, all drugs had similar effects, suggesting that high levels of any psychoactive agent produce a type of stress reaction at the neurophysiological level. In patients receiving barbiturates, the number of spindles per minute of stage two sleep decreased, reflecting the decreasing levels of drug. During high doses of all drugs, there was at least some suppression of eye movements. Overall findings suggest that certain EEG waveforms, and, by implication, brain areas or systems may be differentially affected by various classes of drugs when they are abused. (Journal abstract modified)

225164 Spyker, Joan M. University of Virginia Medical School, Dept. of Anatomy, Charlottesville, VA 22901 Assessing

the impact of low level chemicals on development: behavioral and latent effects. Federation Proceedings. 34(9):1835-1844, 1975.

Evidence is reviewed which suggests that nervous tissue, especially the brain, is more sensitive to many foreign chemical substances than has previously been suspected and that toxic effects may be manifested as subtle behavioral disturbances long before classical symptoms of poisoning become apparent. Early detection of an insidious toxic process may enable prevention or attenuation of harm to humans and other organisms. Evidence also indicates that individuals are more vulnerable to adverse factors during the period of development than at any other time in life. Subtle functional disturbances in organisms exposed while immature may be one of the most sensitive indicators of chemical toxicity. Longitudinal evaluation is required to detect long-term or delayed effects of a particular developmental influence on biological and behavioral functions. Examples from research on the subtle and latent consequences of prenatal and early postnatal exposure to methylmercury are used to illustrate the above principles. 38 references. (Author abstract modified)

225331 Weinstein, Morton R.; Goldfield, Michael D. Department of Psychiatry, University of California, San Francisco, CA 94143 **Cardiovascular malformations with lithium use during pregnancy.** American Journal of Psychiatry. 132(5):529-531, 1975.

A continuing study of infants exposed to lithium carbonate in utero is reported. The 143 cases of lithium use during pregnancy collected by the Register of Lithium Babies show that infants exposed to lithium appear to have a higher than expected ratio of cardiovasulcar anomalies to all anomalies and may have an increased risk of congenital heart disease. These findings justify a conservative policy on the use of lithium with fertile and pregnant women. 17 references. (Journal abstract modified)

225332 Swett, Chester, Jr. Boston Collaborative Drug Surveillance Program, 400 Totten Pond Rd., Waltham, MA 02154 **Drug-induced dystonia.** American Journal of Psychiatry. 132(5):532-534, 1975.

A report is made on the occurrence of dystonia among 1152 psychiatric inpatients who were exposed to a butyrophenone, to a phenothiazine, or to a thioxanthene. Of the 1152 surveyed, 116 developed dystonia attributed to one or more of these drugs. The highest frequencies of dystonia occurred among recipients of haloperidol and the long-acting injectable fluphenazines. For all patients at risk, dystonia was more common in men and in younger patients. For chlorpromazine, high doses, male sex, and low age were each positively associated with dystonia. 7 references. (Journal abstract modified)

225333 Moline, Ronald A. Illinois State Psychiatric Institute, 1601 W. Taylor St., Chicago, IL 60612 **Atypical tardine dyskinesia.** American Journal of Psychiatry. 132(5):534-535, 1975.

An atypical case of tardive dyskinesia in a 19 year old male who had been given relatively low dosages of neuroleptic medication for less than 6 months is presented. The symptoms cleared within 3 months after the medication was discontinued. The literature regarding similar cases is reviewed. Increased reporting and careful description of such cases is suggested as useful for furthering the understanding of this syndrome. 16 references. (Journal abstract modified)

225334 Shopsin, Baron; Gershon, Samuel. Department of Psychiatry, New York University Medical Center, 550 First Ave., New York, NY 10016 **Cogwheel rigidity related to lithium maintenance.** American Journal of Psychiatry. 132(5):536-538, 1975.

A preliminary study of outpatients receiving lithium carbonate maintenance therapy for recurrent affective illness is reported. Most of the patients receiving lithium for more than 8 months had cogwheel rigidity. The data suggest a positive correlation between the duration of lithium maintenance and the severity of cogwheeling. Intravenous administration of benztropine, an antiparkinsonian drug, did not abolish or significantly ameliorate this symptom. 8 references. (Journal abstract modified)

225335 Petti, Theodore A.; Campbell, Magda. New York University Medical Center, 550 First Ave., New York, NY 10016 **Imipramine and seizures.** American Journal of Psychiatry. 132(5):538-540, 1975.

A case is reported of a psychotic preschool child who manifested a seizure disorder while on imipramine treatment. According to the history and physical exam, the child fell within a group that seems predisposed to this side-effect. Although tricyclic antidepressant compounds can be used judiciously with seizure-prone individuals, it is recommended that alternative modalities be given first consideration. 24 references. (Journal abstract modified)

225336 Martin, Gilbert I.; Zaug, Patricia J. Magan Medical Clinic, 420 W. Rowland St., Covina, CA 91722 **Electrocardiographic monitoring of enuretic children receiving therapeutic doses of imipramine.** American Journal of Psychiatry. 132(5):540-542, 1975.

The possible cardiotoxic effect of imipramine treatment for childhood enuresis was examined in a study of the monthly electrocardiographic tracings of 27 children with normal cardiovascular function receiving imipramine therapy for enuresis. No substantial EKG changes were found in any of these children who were receiving doses of 25 to 75 mg of the drug. Electrocardiographic monitoring may be essential only when more than 25 to 75 mg of imipramine are given. It is recommended that the patient's cardiovascular function be established as normal before the drug is administered. 17 references. (Journal abstract modified)

225337 Winsberg, Bertrand G.; Goldstein, Stanley; Yepes, Louis E.; Perel, James M. Child Psychiatric Evaluation Research Unit, New York State Dept. of Mental Hygiene, 524 Clarkson Ave., Brooklyn, NY 11203 **Imipramine and electrocardiographic abnormalities in hyperactive children.** American Journal of Psychiatry. 132(5):542-545, 1975.

Seven cases of electrocardiographic abnormalities occurring in 7 to 10 year old children receiving imipramine pharmacotherapy for behavior disorders are reported. Three children evidenced a first degree atrioventricuolar block. The abnormalities were less pronounced in the other four children. Imipramine plasma levels during steady state were not found to be directly related to the extent of the electrocardiographic changes within the obtained plasma values. Careful clinical surveillance of children receiving imipramine pharmacotherapy is advised. 25 references. (Journal abstract modified)

225338 Lutz, Elmar G. Dept. of Psychiatry, St. Mary's Hospital, Passaic, NJ 07470 **Allergic conjunctivitis due to diazepam.** American Journal of Psychiatry. 132(5):548, 1975.

A report of 4 female patients who developed conjunctival hypersensitivity during diazepam treatment is presented. The hypersensitivity was self-limited after the diazepam was discontinued. It is suggested that until a causative relationship can be established, allergic conjunctival reactions might be erroneously diagnosed as being caused by contact lens irritation in persons wearing contact lenses. 2 references. (Journal abstract modified)

225343 Reda, Fatma A.; Escobar, Javier I.; Scanlan, John M. University of Minnesota Medical School at St. Paul-Ramsey Hospital and Medical Center, 640 Jackson St., St. Paul, MN 55101 **Lithium carbonate in the treatment of tardive dyskinesia.** American Journal of Psychiatry. 132(5):560-562, 1975.

To evaluate the therapeutic effect of lithium on tardive dyskinesia, a study was made of six patients with tardive dyskinesia treated with lithium carbonate in an open clinical trial. Evaluations using a new tardive dyskineia rating scale showed statistically significant improvement in dyskinetic movements while the patients received lithium. This improvement was consistently observed in all patients but was relatively small when compared to the amount of pathology present. 7 references. (Journal abstract modified)

225537 Janz, Dieter. Freie Universitat Berlin, Abteilung fur Neurologie, Klinikum Charlottenburg, Berlin **The teratogenic risk of antiepileptic drugs.** Epilepsia (Amsterdam). 16(1):159-169, 1975.

The inherent teratogenic risk factors and genetic implications in the use of antiepileptic drugs are examined. The frequency of congenital malformations in children of epileptic mothers, such as cleft lip and cleft palate, congenital heart lesions, and various malformation syndromes, are discussed. Conditions independent of drug intake are defined as part of the risk of malformation: genetics and environment. The mechanism of teratogenic effects is outlined, distinguishing between mutagenic and primary genetic anomalies. Recommendations for minimizing teratogenic risk are given. 54 references.

225538 Booker, Harold E. Epilepsy Center, Dept. Neurology, University of Wisconsin Center for Health Sciences, Madison, WI 53706 **Idiosyncratic reactions to the antiepileptic drugs.** Epilepsia (Amsterdam). 16(1):171-181, 1975.

Idiosyncratic drug reactions, defined as adverse drug effects caused by genetically determined enzymatic abnormalities, are studied with particular regard to antiepileptic drugs. Other rare and unusual adverse reactions to the antiepileptic drugs are included, such as drug interactions, drug/disease interactions, drug allergies, and organ toxicities, as well as true idiosyncrasies. Responsibility for initial recognition and later diagnosis of these reactions falls heavily upon the clinician. In addition to discussing the more common or serious rare reactions, the epidemiology and general mechanisms underlying the reactions are discussed. Treatment involves drug withdrawal, plus general supportive and specific therapy determined by the type and severity of the individual reaction. 40 references. (Author abstract modified)

225539 Plaa, G. L. Departement de Pharmacologie, Faculte de Medecine, Universite de Montreal, Montreal, Quebec, Canada **Acute toxicity of antiepileptic drugs.** Epilepsia (Amsterdam). 16(1):183-191, 1975.

The acute toxic effects attributable to antiepileptic drugs are presented. With diphenylhydantoin (DPH), the symptoms are nystagmus, ataxia, and tremors. The effects of primidone are pronounced sedation, vertigo, nausea, diplopia, and nystagmus. Phenobarbitol appears to cause drowsiness, nystagmus, and ataxia. Carbamazepine has side effects of nausea, loss of appetite, gastrointestinal complaints, vision disturbances, decreased psychomotor activity, anxiety, and restlessness. Benzodiazepines induce depression and lethargy. Sulthiame increases the plasma concentration of DPH. Individual cases and a general review of the literature are given. 47 references.

16 METHODS DEVELOPMENT

213595 van Riezen, H.; Behagel, H.; Chafik, M. Organon International B.V., Oss, Holland **Development of psychotropic drugs.** Psychopharmacology Bulletin. 11(2):10-15, 1975.

Some new approaches to the development of psychotropic drugs are discussed. The traditional empirical methods eliminate as useless some compounds which may have useful central effects but which may have a mechanism of action different from that of the known drugs. GB-94 is an example of such a falsely labelled compound. It is suggested that the best approach to detect central nervous system activity is with the commonly used animal batteries supplemented by experiments employing conditioning or EEG techniques and with drug administration over prolonged periods of time. After initial safety studies, the drug should be tested in human volunteers and patients, using computer electroencephalogram analysis and psychometric tests. 5 references.

214812 Dingler, Robert D.; Uhlenhuth, E. H.; Stern, Martin. University of Chicago, Pritzker School of Medicine, 950 East 59th St., Chicago, IL 60637 **SKED program for a modified Sternberg procedure.** Behavior Research Methods & Instrumentation. 7(2):249-250, 1975.

At the Fourth National Conference on the Use of On-Line Computers in Psychology, held in November 1974, a procedure which integrates a number of machine language subroutines within the SKED system was described. This provides a flexible system for controlling sequential events in studies of pharmacological effects on performance of psychomotor tasks by human subjects. A description of the procedure and examples of each subroutine's use were presented. 2 references. (Author abstract modified)

215860 Bunney, William E., Jr.; Murphy, Dennis L. Adult Psychiatry Branch, NIMH, Bethesda, MD 20014 **Strategies for the systematic study of neurotransmitter receptor function in man.** Bethesda, MD, NIMH, 1975. 31 p.

Pharmacological and tissue model strategies for the study of neurotransmitter receptor site function in man are discussed. Pharmacological research strategies involve: 1) the measurement of specific behaviors in man which appear to be changed by alterations in receptor site sensitivity; 2) the utilization of agonists to test changes in receptor site sensitivity; and 3) the utilization of compounds which in themselves increase or decrease receptor site sensitivity, followed by agonists to test for altered sensitivity states. Three possible tissue models are suggested: human subcuntaneous adipose tissue obtained on biopsy may measure alpha adrenergic receptors, and platelets offer a system for studying alpha adrenergic receptors, while human leukocytes provide a model for studying beta adrenergic receptors. The importance of these studies in understanding neuropathology and the pharmacologogical treatment regimens of certain disorders is discussed. 65 references. (Author abstract modified)

217550 Battenberg, E. L. F.; Bloom, F. E. Laboratory of Neuropharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **A rapid, simple and more sensitive method for the demonstration of central catecholamine-containing neurons and axons by glyoxylic acid induced fluorescence: I. specificity.** Psychopharmacology COmmunications. 1(1):3-13, 1975.

A method for demonstration of central catecholaminergic contain neurons and axons is described. Perfusion fixation with a mixture of paraformaldehyde and glyocylic acid facilitates the histochemical demonstration of catecholamine containing brain neurons. With this fixation, sections can be cut reproducibly with a cryostat and the fluorophore developed by immersion in glyoxylic acid without freeze drying. Large sections of brain can be examined by fluorescence microscopy with I hour of fixation or stored for later examination. The properties of the fluorophore and the location of the fluorescent elements is identical with the neurons and terminal arborizations demonstrated by previous glyoxylic acid methods. Monoamine oxidase inhibition before fixation results in moderately increased fluorescence of terminals and perikarya, while all glyoxylic acid induced fluorescence is abolished by pretreatment with reserpine. The rapidity and simplicity of this technique may make fluorescence histochemistry of central catecholamine pathways more accessible to psychopharmacologists. 15 references. (Author abstract)

217666 Dixon, W. R.; Earley, J.; Postma, E. Department of Biochemistry and Drug Metabolism, Hoffmann-La Roche Inc., Nutley, NJ 07110 **Radioimmunoassay of chlordiazepoxide in plasma.** Journal of Pharmaceutical Sciences. 64(6):937-939, 1975.

A simple, rapid, and sensitive radioimmunoassay was developed for the determination of chlordiazepoxide (7-chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine 4-oxide) in plasma. Antiserum capable of binding chlordiazepoxide-2-14C was obtained from rabbits following immunization with an antigen prepared by coupling the reactive acyl azide of 7-chloro-5-(4-hydrazinocarbonylmethoxyphenyl)-2-methylamino-3H-1,4-ben odiazepine 4-oxide to bovine serum albumin. The radioimmunoassay allows for the specific determination of chlordiazepoxide directly in plasma without extraction and was compared with a different spectrofluorometric assay for chlordiazepoxide. Both methods gave satisfactory agreement for the plasma levels of chlordiazepoxide in human subjects resulting from single and chronic oral doses of chlordiazepoxide hydrochloride. 9 references. (Author abstract)

218042 Stallone, F.; Mendlewicz, J.; Fieve, R. R. New York State Psychiatric Institute, 722 West 168th St., New York, NY 10032 **Double-blind procedure: an assessment in a study of lithium prophylaxis.** Psychological Medicine (London). 5(1):78-82, 1975.

The efficacy of a double-blind controlled procedure in a study of lithium prophylaxis is reported. Fifty seven patients with primary affective disorder were questioned as to whether they believed they were receiving lithium or placebo. Research nurses and a close relative living with each S were also questioned. Nearly all, 96%, said they believed they were receiving lithium, ascribing this belief in 63% of the cases to a perceived improvement in condition. In 14% of the Ss on lithium the presence of side-effects were implicated in the patients' beliefs. One of the three nurses had a correct guess rate in excess of chance expectancy. All nurses tended to be more accurate in their guesses in the cases of Ss who had been in prophylactic trials of over 15 months' duration than for Ss with briefer periods in the study. As a group, patients' relatives were extremely accurate in their correct guess rate, exceeding chance rate at the .001 level. 5 references. (Author abstract modified)

221288 Bente, D.; Feder, J.; Helmchen, H.; Hippius, H.; Rosenberg, L. no address /**Double-blind test of three antidepressants, third communications: methodological problems.**/ Doppelblindprufung von drei Antidepressiva, E. Mitteilung: Methodische Probleme. Arzneimittel-Forschung (Aulendorf). 24(2):205-207, 1974.

The results of a double-blind study with the antidepressants noxiptiline, nornoxiptiline and amitriptyline in 149 patients with mixed diagnoses are reported graphically. The findings are discussed critically with regard to the methodology. The introduction of the AMPAS program system for processing AMP data shows great promise over traditional methods. While it has become possible to compute the level of significance of each item at each moment with the AMPAS system, it is still necessary to critically discuss new findings with regard to the methods used before interpreting their clinical meaning. 8 references. (Journal abstract modified)

224894 Struening, Elmer L.; Shapiro, Arthur K.; Shapiro, Elaine. Columbia University School of Public Health, New York, NY **Reliability and validity of a placebo test.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 240-241).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, a paper was presented reporting the results of a test to determine the reliability, validity, and structural invariance of a placebo test (PT) to measure changes in current symptoms, development of new symptoms or side-effects, and overall placebo effect. A group of 1800 psychiatric outpatients were evaluated with a comprehensive battery of self-report inventories, rating scales, and tests and their reaction to three placebo situations was measured via the PT. By applying factor analysis, two dimensions of placebo reaction were clearly identified: the placebo effect factor (PEF), and the side-effects factor (SEF). The former measured the overall effects after the ingestion of a drug placebo and change in current symptoms or which Ss brought to the placebo testing situation; the latter measured the presence of new symptoms. Results confirm the reliability, concurrent validity, and predictive validity of the PT. Its structural invariance was also demonstrated. (Journal abstract modified)

225517 Schweitzer, Jack W.; Friedhoff, Arnold J.; Schwartz, Ralph. Millhauser Laboratories of the Dept. Psychiatry, New York University School of Medicine, New York, NY **Phenethylamine in normal urine: failure to verify high values.** Biological Psychiatry. 10(3):277-285, 1975.

To test the presence of phenethylamine (PEA) as an indicator for various psychotic disturbances, the PEA level in daytime urine samples of 18 normal subjects was measured by an isotope dilution technique. Purification of PEA from other urinary substances, after the addition of 1-14C-PEA to urine samples, was achieved by the sequence: thin layer chromatography (TLC), derivatization, TLC, and finally, gas chromatography (electron capture). A circadian rhythm was not evident on the basis of analyses of 24hr urine collections from four normal subjects. Three acute schizophrenics had levels within the normal mean. Implications of the test results are discussed. It is concluded that reported findings relating PEA excretion

to various psychiatric disturbances is premature. 14 references.
(Author abstract modified)

17 MISCELLANEOUS

213392 Denber, Herman C. B. University of Louisville, Louisville, KY 40208 **Psychopharmacological treatment: theory and practice.** Modern Pharmacology-Toxicology Series. New York, Marcel Dekker, 1975. 312 p. Vol. 2. $19.75.

The technological aspects of psychopharmacology are discussed. The importance of a complete scientific grounding to the proper application of psychopharmacological treatment is stressed. The indications, limitation, and specific contraindications of various psychotropic drugs are discussed. Clinical applications and effects are examined in order to provide the basic information that is necessary to achieve the best results in psychopharmacological treatment.

213597 Bobon, D. P.; Bourdouxhe, S. Department of Psychiatry, University of Liege Medical School, Liege, Belgium **New psychotropic drug developments in France and Belgium.** Psychopharmacology Bulletin. 11(2):19-23, 1975.

Recent psychotropic drug developments in France and Belgium are discussed, emphasizing two recent trends: endocrinology (illustrated by the thyrotropin releasing hormone), and integrative processes and aging (illustrated by piacetam). The interrelations between endocrinology and psychiatry have led to the development of the field of psychoendocrinology. The search for drugs to counteract the process of aging has been hampered by the difficulty in measuring the effects of such drugs. The development of new antidepressants, particularly bicyclic and tetracyclic derivatives, is considered. It is noted that a higher therapeutic index and greater specificity of action constitute constant goals for psychopharmaceutical research. The development of new preparations aimed at better manipulation or at longer duration of action is considered. The controversy between clinical experimenters and government agencies over the regulation of new drug testing is elucidated. 11 references.

213599 Wheatley, David. General Practitioner Research Group, Twickenham, England **New psychotropic drug developments in Great Britain.** Psychopharmacology Bulletin. 11(2):28-31, 1975.

Research in psychopharmacology in Great Britain is discussed and described under four headings: the mechanisms of drug effects; development of new antidepressants of original chemical formulation; the use of nonpsychotropic drugs to treat depression and anxiety; and psychotropic drugs in physical disorders. Recent research has concentrated on the plasma levels of tricyclic antidepressants. Other areas discussed include the use of nonpsychotropic drugs and anxiety and hypertension. 5 references.

213600 Simeon, Jovan; Utech, Carla; Simeon, Susan. Missouri Institute of Psychiatry, School of Medicine, University of Missouri-Columbia, St. Louis, MO 63121 **Twenty-three psychotropic drugs used in children abroad which are not recommended in the United States.** Psychopharmacology Bulletin. 11(2):31-38, 1975.

Twenty three drugs named by survey respondents from 25 countries as being used for treatment of psychological disorders in children were tabulated. Each drug was selected by one or more respondents as one of his three choices for the treatment of one or more of the following disorders: hyperkinetic reaction, unsocialized aggressive reaction, overanxious reaction, withdrawing reaction, psychosis, insomnia, sleepwalking, nightmares, enuresis, obsessive-compulsive neurosis, and phobic neurosis. The drugs are classified according to their effect on adults and by generic name, followed by one or more of their trade names. 5 references.

213715 Costa, E.; Gessa, G. L.; Sandler, Merton. no address **Serotonin -- new vistas: histochemistry and pharmacology.** Advances in Biochemical Psychopharmacology. New York, Raven Press, 1974. 320 p. Vol. 10. $19.75.

The histochemistry and pharmacology of serotonin are reviewed. The relationships between serotonin and sleep, sexual behavior and aggressive behavior are considered. The roles of serotonin in memory and in the development of schizophrenia are evaluated.

213716 Costa, E.; Gessa, G. L.; Sandler, Merton. no address **Serotonin -- new vistas: biochemistry and behavioral and clinical studies.** Advances in biochemical psychopharmacology. New York, Raven Press, 1974. 418 p. Vol. 11. $19.75.

The role of serotonin in biochemical pharmacology is discussed. The use of serotonin in the study of the distribution of sertonergic brain pathways is outlined. The metabolic pathways invoved in the N-demethylation of the indoleamines and the role of tyrosine hydroxylase in the synthesis of serotonin are considered. The use of affinity chromatography in the investigation of serotonin binding proteins is described.

213919 Davidson, Jonathan R. T.; Raft, David; Lewis, B. Frank; Gebhardt, Margaret. School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC 27514 **Psychotropic drugs on general medical and surgical wards of a teaching hospital.** Archives of General Psychiatry. 32(4):507-511, 1975.

The prescribing habits for psychotropic drugs of internists, surgeons, and gynecologists on their inpatient wards in a teaching hospital were studied from patients' charts and pharmacy records. In a 6 week period, 9% of all admissions received such a drug. The maximum incidence of receiving these medications was in the 50-year-old to 60-year-old age group. Minor tranquilizers were prescribed most frequently, followed, respectively, by major tranquilizers, barbiturates, and antidepressants. Less than half the available drugs were used, but drugs of different groups were often used interchangeably in an unsystematic fashion, and there was little evidence as to how effective a drug had been. It also seemed that depression was often overlooked or insufficiently treated. 22 references. (Author abstract modified)

213920 Greenblatt, David J.; Shader, Richard I.; Koch-Weser, Jan. Boston Collaborative Drug Surveillance Program, 400 Totten Pond Road, Waltham, MA 02154 **Psychotropic drug use in the Boston area: a report from the Boston Collaborative Drug Surveillance Program.** Archives of General Psychiatry. 32(4):518-521, 1975.

As part of the Boston Collaborative Drug Surveillance Program, adults admitted to general medical and surgical wards in Boston area hospitals in 1972 were interviewed to determine their use of prescribed psychotropic drugs prior to hospitalization. Patients hospitalized for psychiatric disorders or psychogenic ("functional") disease were excluded. Patients who had taken prescribed drugs that could not be identified were considered nonusers. Of the total sample, 20% gave a

history of psychotropic drug use. Antianxiety drugs were taken by 15% of the patients and accounted for two thirds of total psychotropic drug use. Hypnotics were taken by another 4% of the sample. Slightly over half of antianxiety and hypnotic drug use was for a year or more. Use was more frequent in patients with potentially chronic medical disorders. The findings, in general, are consistent with other studies using other methods to investigate the use of psychotropic drugs. 34 references. (Author abstract modified)

214228 Morris, Louis Allen. Tulane University **Behavioral and physiological feedback as sources of information about the "effectiveness" of a placebo. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-2941 HC$13.50 MF$5.00 51 p.

The manner in which persons integrate information in order to judge the effectivness of a drug they have taken was studied in male undergraduates. Ss received a placebo, but were either told that the drug should increase their physiological arousal or their visual concentration. They received bogus feedback regarding their pulse rate and pursuit rotor performance. Half received feedback indicating that their rotor performance had improved and half that it did not change relative to a prepill baseline. The same procedure was followed for feedback instructions on pulse rate. As predicted, Ss expecting a behavioral change relied on the pursuit rotor feedback, but also accepted a pulse rate increase an in indicator of the drug's effectivness. Those expecting a physiological reaction relied on their pursuit rotor performance to a greater extent if their heartrate increased than if it remained the same. The possibility that the pulse rate increase feedback confirms expectancy if the drug induction stresses behavioral drug effects, but creates uncertainty about its effectiveness if the induction stresses physical effects, is raised. (Journal abstract modified)

214337 Morris, David J. Department of Laboratory Medicine, The Miriam Hospital, Providence, RI **Drug metabolism and therapeutic monitoring.** Rhode Island Medical Journal. 57(11):461-463, 481, 1974.

An overview is conducted of new technical procedures that will permit accurate assays of the proper levels of therapeutic drugs in individual patients. It is described how the findings of the many studies that have been performed on the absorption, distribution, binding or localization in tissues, metabolism, and excretion of drugs are being utilized in the measurement of therapeutic levels of drugs in the blood. The wide range of dosages required in different individuals for the maintenance of similar clinical states can now be better understood through examination of drugs' routes of absorption, distribution, metabolism and excretion. 12 references.

214341 Engelhardt, David M. Psychopharmacology Research Unit, State University of New York, Downstate Medical Center, Brooklyn, NY **Ethics in medical research as viewed by the clinical investigator.** Connecticut Medicine. 38(12):680-682, 1974.

The complexities of the extensive testing required to determine if a drug is safe and clinically effective are outlined. The following points are made in regard to clinical investigation with experimental drugs: (1) despite occasional tragedies, experimentation with drugs has proven remarkably safe; (2) written informed consent is a relative term because there are limits to patient comprehension of what the clinical investigator is attempting; (3) the patient volunteering for drug research in not doing the clinical investigator a favor because such experimentation is in the public's interest; and (4) public scrutiny of clinical investigators must not be allowed to destroy his freedom to work.

215074 Lapin, I. P. Laboratory of Psychopharmacology, Bekhterev Psychoneurological Research Institute, Leningrad **Antagonism of nicotine acid and other kynurenines to antidepressants: one of the probable reasons for the therapy-resistance in depression?** Activitas Nervosa Superior (Praha). 16(4):260-261, 1974.

At the 16th Annual Psychopharmacological Meeting, Jesenik, 1974, a paper was presented which reported the influence of injected kynurenines and inhibition of liver tryptophan pyrrolase on pharmacological effects of antidepressants. Data on nicotinic acid suggest that it is likely that increased formation of kynurenines in depressive patients with anxiety, tension or fear can antagonize the pharmacological effects of side-effects and that this antagonism can be one of the probable reasons of therapy resistance in depression. Systematic experimental and clinical investigation is advocated. 9 references.

215251 Evenson, Richard C.; Altman, Harold; Cho, Dong Won; Sletten, Ivan W. Missouri Institute, U. of Missouri School of Medicine, St. Louis, MO **The relationship of diagnosis and target symptoms to psychotropic drug assignment.** Comprehensive Psychiatry. 15(2):173-178, 1974.

Methods employed to extend and improve a computer's ability to predict the assignment of psychotropic drugs are examined. Data are drawn from computer files on 3,314 patients from five state hospitals and three urban mental health centers who were assigned to only one of 10 specified psychotropic drugs. Results indicate that clinician's diagnosis influences his drug choice more than does his observation of target symptoms or mental status. Minor tranquilizers are shown to be related to diagnosis of alcoholism, while antidepressants are related to diagnosis of depression or suicidal thoughts. It is suggested that clinical consensus limits the hit rate that can be demonstrated by computer assignment in the area of 75% to 80% maximum accuracy. 17 references.

215291 Yagi, Kohei; Yoshida, Hiromune; Takagi, Shuichiro. Minakawa Hospital, Kanagawa Prefecture, Japan **Psychotropic drug therapy in a mental hospital.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(2):205-216, 1974.

The status of psychopharmacotherapy at two Japanese mental hospitals is discussed. The public hospital treated primarily outpatients who suffered from epilepsy, neuroses, hypertension, and vascular disturbances. The preferred mode of treatment there was the administration of antianxiety agents. The private psychiatric hospital treated mostly schizophrenic inpatients and administered primarily anti-Parkinsonism drugs. 6 references.

215680 Taylor, Michael J. Department of Psychiatry, University of California, Davis, CA **Lithium use in manic-depressive illness: practical aspects.** Journal of the Iowa Medical Society. 65(5):180-182, 1975.

The value of lithium carbonate in both the treatment and prevention of episodes of illness in properly diagnosed patients with manic depressive illness is discussed. Consideration is given to dosage determinations, use of lithium in acute mania, prophylactic lithium, toxicity and contraindications. Of vital importance is the proper monitoring of serum levels and the maintenance of the serum level at between 0.8and 1.2mEq/L if

the drug is to be therapeutically effective. 10 references. (Author abstract modified)

216706 Kline, Nathan S. Columbia University College of Physicians and Surgeons, New York, NY **From sad to glad: Kline on depression.** New York, G. P. Putnam's Sons, 1974. 256 p. $7.95.

Types of depression and their diagnosis and treatment are discussed; and the social history of depression is outlined. Medical research involved in tracing causes and cures is reviewed, and certain misapplications of psychoanalytic methods are criticized. The chemical processes of the brain and the function of antidepressant drugs on it are detailed. Depression in the aged, suicide, alcoholism and drug addiction are also given special consideration.

216948 Howie, J. G. H. University of Aberdeen, Aberdeen AB9 2ZD, England **Psychological medicine: psychotropic drugs in general practice.** British Meical Journal (London). No. 5964:177-179, 1975.

An overview of the problem of general practitioners prescribing psychotropic drugs is treated in three subject categories: 1) the variation in the habits of general practitioners prescribing hypnotic drugs, including the questions of patient preference and the use of a new drug to replace the old; 2) the range of the doctor's ability and knowledge of psychotropic drugs; and 3) the high risks of side-effects of psychotropic drugs. Other topics include iatrogenic disorders from polypharmaceutical practices, combined preparations, and interactions between drugs being used simultaneously. It is suggested that a smaller range of drugs be made available to general practitioners, allowing patients to receive drugs more familiar to the doctor which will reduce inappropriate medication and side-effects. 5 references.

218150 Gluckman, Melvyn I. Research Division, Wyeth Laboratories, Radnor, PA **Summary of the animal pharmacology of oxazepam.** Diseases of the Nervous System. 36(5, Section 2):4-5, 1975.

The animal pharmacology of oxazepam, a member of the 1,4-benzodiazepine class of compounds, is summarized. Data suggest that oxazepam has relatively specific antianxiety effects, its sedative - hypnotic and muscle relaxant properties being relatively minor. The short half-life of the compound suggests an ease of reversibility of effect which is demonstrated in conflict studies. 8 references. (Author abstract modified)

218151 Greenblatt, David J.; Shader, Richard I.; Koch-Weser, Jan. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **Pharmacokinetics in clinical medicine: oxazepam versus other benzodiazepines.** Diseases of the Nervous System. 36(5, Section 2):6-13, 1975.

The pharmacokinetics of oxazepam and possible clinical implications of differences between oxazepam and other benzodiazepine derivatives are discussed. Findings suggest that although the neuropharmacologic effects of chlordiazepoxide, diazepam, oxazepam and clorazepate are probably very similar, the unique pharmacokinetic properties of oxazepam may impart to this drug a special role in clinical practice. When short acting, rapidly terminating, nonaccumulating clinical effects are desirable, oxazepam is the benzodiazepine derivative most likely to meet these requirements. 48 references. (Autnor abstract modified)

218152 Ayd, Frank J., Jr. Taylor Manor Hospital, Ellicott City, MD 21043 **Oxazepam: an overview.** Diseases of the Nervous System. 36(5, Section 2):14-16, 1975.

Data on oxazepam gathered from 10 years of worldwide clinical experience is analyzed; it is concluded that treatment of thousands of patients demonstrates that oxazepam is a valuable and safe drug with a wide range of clinical usefulness. It is now evident that all benzodiazepines are not the same, and oxazepam has properties that appear useful, especially for neurotic and geriatric patients. 20 references. (Author abstract modified)

218154 Blackwell, Barry. Dept. of Psychiatry, University of Cincinnati Medical Center, Cincinnati, OH 45267 **A critical review of oxazepam: efficacy and specificity.** Diseases of the Nervous System. 36(5, Section 2):17-22, 1975.

Clinical data relating to the effects of oxazepam are reviewed. The effectiveness of the drug for treating anxiety in patients, in support of animal data, was confirmed in 14 out of 17 comparisons with placebo in controlled double-blind experiments. The fact that the drug has not become more widely used is attributed to the failure to differentiate it adequately from other benzodiazepines. The possibility suggested in animal studies that oxazepam might produce relatively less sedation than chlordiazepoxide and therefore have specific advantages in the elderly has not been sufficiently explored in a manner capable of either confirming or refuting the hypothesis. 33 references. (Author abstract modified)

218582 Schaller, J. P. 10, rue de Montjoie, 2900-Porrentruy, Switzerland **/Psychopharmacology and morals./** Psychopharmacologie et morale. Vie Medicale au Canada Francais (Quebec). 4(1):56-63, 1975.

Moral aspects of psychopharmacology are discussed, focusing on the psychosomatic problem. Disciplines concerned with psychosomatic problems have an important place in human sciences. Psychopharmacology is a science and its application is an art that the physician must learn. The moralist must equally "learn" morals: it is a discipline whose principles and rules must be learned. Treatment may involve psychiatric care or chemotherapy; it is in this way that priest and physician collaborate for man's well-being, each playing his respective role -- a distinct, parallel but not opposed action. 25 references.

219756 Cox, Richard H. La Jolla, CA **II. Psychopharmacology and the nonmedical practitioner.** Professional Psychology. 6(2):169-171, 1975.

A rudimentary knowledge of psychopharmacology is deemed essential for the professional practitioner of psychotherapy. Advantages of a greater knowledge of pharmacology to the nonmedical practitioner are outlined, and the need for every professional to recognize the limits of his or her competence and legal capacity is stressed.

219970 Sturges, Stanley; Brown, Marian. Kettering, OH **Polypsychopharmacy.** Bulletin of the Menninger Clinic. 39(3):274-279, 1975.

The practice of the administration and prescription of multiple drugs to general patients was investigated. Psychotropic drug prescription patterns were studied in three general hospital psychiatric units. It was discovered that two of three hospitals used multiple medications, and the extent of use of combinations of psychotropic and antipsychotic drugs is assessed. The uncertainty involved in the use of antiparkinson

agents is noted, and errors in drug administration and patient noncompliance are considered. 13 references.

220311 Iverson, Leslie L. M.R.C. Neurochemical Pharmacology Unit, Dept. of Pharmacology, Univ. of Cambridge, Cambridge CB2 2QD, England **Dopamine receptors in the brain.** Science. 188(4193):1084-1089, 1975.

The significance of a dopamine sensitive adenylate cyclase in the central nervous system is discussed in relation to the expanded treatment possibilities of antipsychotic drugs. Evidence from studies that establish the extreme sensitivity of dopamine sensitive adenylate cyclase in mammalian central nervous systems to inhibition by antipsyhcotic drugs is reviewed. The possibility of the antagonistic effects of antipsychotic drugs on presynaptic mechanisms as well as on postsynaptic dopamine receptors is also considered. The symptoms associated with Parkinson's disease that are caused by antipsychotic drugs are described. It is concluded that the biochemical and pharmacological study of dopamine receptors may prove helpful in leading to new and highly specific pharmacological tools that may assist in future studies of the functional role of dopamine in the central nervous system. 47 references.

220403 Vovin, R. Ya.; Vovina, E. N.; Malakhov, B. B.; Khvilivitskiy, T. Ya. Leningradskiy nauchno-issledovatel'skiy psikhonevrologicheskiy institut im. V. M. Bekhtereva, Leningrad **/Clinical - psychopathological criteria for the selection of psychotropic drugs according to the stage of illness and the effectiveness of rehabilitating schizophrenics./** Etapnyye kliniko-psikhopatologicheskiye kriterii vybora psikhotropnykh sredstv i effektivnost' reabilitatsii bol'nykh shizofreniyey. In: Kabanov, M., IV Mezhdunar. Simpoz. po Reabilit. Psikhicheski Bol'nykh. Leningrad, Psikhonevrologicheskiy Institut, 1974. 331 p. (p. 144-148).

In a paper presented at the Fourth International Symposium on Rehabilitation of the Mentally Ill held in Leningrad, October 1974, the combined use of drug therapy and sociopsychological therapy was examined and evaluated. Types of drugs which can be effectively used at each stage of therapy were detailed. Treatment outcome data for 253 patients were included. (Journal abstract modified)

221075 Thornton, William E.; Pray, Bonnie J. Dept. of Medicine, Illinois Drug Abuse Programs, State Department of Mental Health, 1440 S. Indiana Ave. Chicago, IL 60605 **Combination drug therapy in psychopharmacology.** Journal of Clinical Pharmacology. 15(7):511-517, 1975.

Clinical and theoretical knowledge bearing on combination drug therapy is reviewed, and the frequency with which a psychotropic agent is used in combination with another drug preparation is emphasized. Drug combination interactions that enhance clinical efficacy and those that either diminish it or even endanger the patient are described. It is suggested that any unexpected or unusual drug action should be examined for the possibility of a drug combination interaction. 49 references. (Author abstract modified)

221563 Cole, Jonathan O. Psychiatry Dept., Harvard Univ. Medical School, Boston, MA **What's in a word? or guilt by definition.** Massachusetts Journal of Mental Health. 5(2):4-13, 1975.

Semantic problems related to the concepts of behavior modification and psychotropic drugs are examined. Parental discipline, societal taboos, education, and prison treatment are cited as examples of behavior modification. It is suggested that good rehabilitation programs are called rehabilitation and bad ones are called behavior modification. Appropriate use of psychotropic drugs, such as diazepam or chlordiazepoxide, is advocated as an effective treatment method in certain instances, but the potential for abuse is noted, especially in prisoner programs. It is concluded that restraint and judgment are needed in both the use and interpretation of the phrases behavior modification and psychotropic drugs.

221668 Poirier-Littre, M.-F.; Longevialle-Henin, R.; Joly, H.; Ginestet, D.; Deniker, P. Service Hospitalo-Universitaire de Sante Mentale et de Therapeutique, Paris **/Attempts to classify and orient prescription of psychotropic drugs by means of a computer card index./** Essais de classification et d'orientation de la prescription au moyen d'un fichier des medicaments psychotropes en ordinateur. Encephale (Paris). 1(2):113-120, 1975.

At the 9th International Congress of Neuropsychopharmacology, Paris, July 1974, a paper was presented in which computer card classification of psychotropic drugs belonging to the neuroleptic class was described. Standard profiles were determined according to Belson's method (partially modified). The neuroleptics were analyzed according to two principal variables: the disinhibiting action and the powerful sedative action. The remaining variables were classified as a function of their connection with the principal variable; they were termed explanatory variables and determine the profile of the product. The results are presented in four forms. The use of the computer card index is oriented toward determining objective criteria for classifying these therapeutic agents. It should allow, on the level of daily practice, better estimation of indications and contraindications. 9 references. (Author abstract modified)

221672 Ginestet, D.; Secret, Ph.; Deniker, P. Service Hospitalo-Universitaire de Sante Mentale et de Therapeutique, Paris **/Long-acting drugs in psychiatric treatment: lacunae and needs./** Les medicaments d'action prolongee en therapeutique psychiatrique: lacunes et besoins. Encephale (Paris). 1(2):161-164, 1975.

At the 9th International Congress of Neuropsychopharmacology, Paris, July 1974, a paper was presented in which various aspects of treatment with long-acting drugs such as neuroleptics and antidepressants were discussed. The long-acting neuroleptic (LAN) should possess a broad spectrum of activity, and only have a subdued sedative effect. There are not yet any LANs whose hallucinolytic action is comparable to that of haloperidol. It would be helpful to have products whose action lasts for 24 or 48 hours. The toxicity of antidepressants, especially on the cardiac level, poses problems which are difficult to solve. Research is currently being directed toward obtaining long-acting antiparkinsonian correctors and to obtain some form of lithium salts which would permit a stable nyctohemeral lithium rate after one dose. 6 references.

222411 Lipman, Ronald S. NIMH, Rockville, MD **Results of a survey (1966-1967) of drug usage in institutions for the mentally retarded. (Unpublished paper).** Rockville, MD, NIMH 1975. 35 p.

Drug usage patterns in 109 institutions for the mentally retarded are reviewed as surveyed in 1966-1967. Certain drugs and drug classes were excluded: benadryl, barbiturates, hypnotics, drug combinations (e.g.,Triavil and Deprol), anticonvulsants, and antiparkinson agents. The survey format did not permit an identification of the number of patients receiving a

particular drug dosage nor did it permit cross tabulation of dosage by length of administration, age, sex, or reasons for administration. Drug usage was related to institutional size. At the extremes of resident population (e.g.,below 500 and more than 3000), there was some tendency for larger institutions to use drugs more freely and on a more chronic basis. These differences were not very pronounced. Results indicate that too many mentally retarded residents are receiving phenothiazines, at too high dosages and for too long periods of time. Reform measures are suggested. 31 references.

222602 Johnson, D. A. W. Crumpsall Hospital, Manchester 8, England **Observations on the dose regime of fluphenazine decanoate in maintenance therapy of schizophrenia.** British Journal of Psychiatry (London). 126:457-461, 1975.

An analysis of the drug regimes prescribed to two separate groups of unselected schizophrenic patients is presented, indicating certain trends of clinical importance. The results demonstrate a need for the adoption of a personalized dose regime. The scatter of dose regimes found effective is too great to recommend a standardized approach to the prescription of long-acting phenothiazine injections. Two other results of particular significance are that the dose of drug required to control symptoms can be gradually reduced in nearly half of patients, and that helpful trends in prescribing were identified that will help the clinician to abolish side-effects. 9 references. (Author abstract)

223949 Webb, Stephen D.; Collette, John. University of Victoria, Toronto, Ontario, Canada **Urban ecological and household correlates of stress-alleviative drug use.** American Behavioral Scientist. 18(6):750-770, 1975.

The effects of variations in sociological - spatial variables on stress alleviative drug use among the urban population of New Zealand were examined. Two variables exhibited clear and consistent results: in - dwelling crowding operates as a strong negative predictor of each index of stress, while isolation, or persons living alone, has even greater predictive power and is positively related to each stress measure. While many recent studies have begun to question the notion that urban crowding is a peculiarly noxious condition, none have suggested that it might have a negative impact on stress levels. The data herein, however, support the notion that in - dwelling crowding does not constitute a stressful condition, although it may through some other mechanisms, lend to certain social pathologies. The strong relationship between isolation and stress is consistent with the literature suggesting that isolated persons suffer more physiological and psychological disorders. Some methodological difficulties which should be considered when analyzing the findings are mentioned. 27 references. (Author abstract modified)

224353 Beaton, John M. Department of Psychiatry, University of Alabama, Birmingham, AL 35233 **Methylation & schizophrenia.** Alabama Journal of Medical Sciences. 12(2):193-202, 1975.

The theory of transmethylation, one of the many proposed biochemical hypotheses for the causes of schizophrenia, is considered. A survey of the literature and genetic factors in the etiology of schizophrenia is reviewed. The relationship of methylation to mental illness involves four types of reaction: N-methylation, O-methylation, competitive transmethylation and demethylation. Previous studies on the behavior disturbing effects of methionine and its metabolites and the behavioral effects of L-methionine and related compounds are summarized. It is concluded that exacerbation of schizophrenic symptoms by methionine may not be due to a direct increase in the levels of a methylated psychotoxin, maintained by the transmethylated hypothesis. Suggestions for future research using methionine and serine with schizophrenic patients are presented. 92 references.

224359 Loney, Jan; Ordona, Truce T. Department of Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242 **Using cerebral stimulants to treat minimal brain dysfunction.** American Journal of Orthopsychiatry. 45(4):564-572, 1975.

Questions are considered which were raised during a study of the medical records of 135 boys treated with central nervous system stimulants for minimal brain dysfunction. The questions include: 1) whether physician factors contribute to child diagnosis, treatment choice, and clinical improvement; 2) the definition of improvement; 3) what kinds of and how frequently side-effects occur; and 4) indications for the use of cerebral stimulants 18 references. (Author abstract)

224491 Whitlock, F. A. Department of Psychiatry, Royal Brisbane Hospital, Queensland, Australia 4029 **Suicide in Brisbane, 1956 to 1973: the drug-death epidemic.** Medical Journal of Australia (Sydney). 1(24):737-743, 1975.

Suicide deaths in Brisbane, Australia, from 1966 to 1973 were studied to determine to what extent changes in drug prescribing have played a part in bringing about alterations in suicide rates. The sharp rise in deaths from barbiturate overdosage reached a peak in the mid-1960s: since then there has been a steady decline in suicide rates from drug overdose and a smaller fall in the rate of other forms of suicide. The decline in deaths from carbon monoxide poisoning since 1967 may be due to the use of nontoxic domestic gas. The frequent association between barbiturate suicide and previous ingestion of alcohol indicates the danger of the practice and the probability that many of the victims had major drinking problems. An examination of the prescribing of barbiturates, benzodiazepines, and antidepressant drugs between 1962 and 1973 suggests that the fall in suicide rates was due to the better recognition and treatment of depressive illnesses and to the introduction of safer benzodiazepines in place of barbiturates. The data suggest that the placement of restrictions on nonviolent methods of suicide does not necessarily result in an increase of violent suicides. 13 references. (Author abstract modified)

224492 Mant, Andrea. 42 Mackellar Crescent, Cook, Australian Capital Territory, Australia 2614 **Determinants of prescribing of psychoactive drugs by general practitioners.** Medical Journal of Australia (Sydney). 1(24):743-749, 1975.

A model to determine the crucial elements (age, social background, work load, nature of practice, education, and colleague networks) in the prescribing and usage of psychoactive drugs by general practitioners is presented, and the data from a pilot study in Canberra, Australia, are given. The implications of the model are discussed, and the use of a questionnaire in testing some of the variables is outlined. 34 references. (Author abstract modified)

224742 Diamond, Herbert; Tislow, Richard; Synder, Thoburn; Rickels, Karl. West Philadelphia Community Mental Health Consortium, Philadelphia, PA **Peer review of prescribing patterns in a CMHC.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 58).

At the 128th Annual Meeting of the American Psychiatric Association, held at Anaheim, California in May 1975, a paper was presented in which the need for peer monitoring of the prescribing habits of a dispersed staff of psychiatrists in a decentralized community mental health center (CMHC) was discussed. Results of such a review at seven outpatient counseling centers in the Philadelphia area were reported. The goal was to improve prescribing skills, upgrade care and reduce costs where possible, as well as enhance continuing education. A formal medication review committee was formed, members of which were mandated to raise such questions as a rationale for polypharmacy, duplication of antipsychotic agents, or long-term anticholinergic medication. A nonthreatening statement was sent every month to each psychiatrist feeding back the views of the committee on such issues. Comparison of a sample prescribing period with a control period one year earlier indicated that prescribing patterns had changed. Although several psychiatrists initially felt threatened by the peer review, those concerns were resolved spontaneously because of the noncritical format, emphasizing educational goals and use of tact. This experience also has relevance for Professional Standards Review Organizations and CMHC accreditation. (Journal abstract modified)

224790 Carpenter, William T., Jr.; McGlashan, Thomas H.; Strauss, John S. Psychiatric Assessment Section, Clinical Research Unit, Adult Psychiatry Branch, NIMH, Rockville, MD **Psychosocial treatment of acute schizophrenia.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, DC, American Psychiatric Assn., 1975. 354 p. (p. 121-122).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, May 1975, a paper was presented which described a medical model treatment program for acute schizophrenia based on self-understanding and learning of social skills set in a therapeutic community. What was regarded as therapeutic was specifically identified. Management and treatment of flagrantly psychotic patients in this contact was illustrated with clinical vignettes, and the advantages and disadvantages of antipsychotic medication, used in half of the patients, were discussed. Experience to date provided a basis for defining a psychosocial therapeutic approach, assessing the use of drug intervention in that context, noting patients' ideas about their treatment, and comparing outcome with a conventionally treated schizophrenic cohort. Findings support the view that the polarization around schizophrenic treatment is unwarranted, and ethical issues recently raised regarding withholding medication from schizophrenics were felt to be presumptive. (Journal abstract modified)

224829 Harazti, Joseph; Jones, Frank; Garver, David L.; Davis, John M. Illinois State Psychiatric Institute, Chicago, IL **Clinical pharmacology in psychiatry.** In: Scientific proceedings in summary form: 128th annual mtg., APA. Washington, American Psychiatric Assn., 1975. 354 p. (p. 163-164).

At the 128th Annual Meeting of the American Psychiatric Association, held in Anaheim, California, in May 1975, a paper was presented reviewing the history of clinical pharmacology and psychiatry in general medicine. Focus was on the relationship of plasma levels to therapeutic effects and to side-effects of various compounds used in treating psychiatric illness, including chlorpromazine and butaperazine. (Journal abstract modified)

224972 Swazey, Judith P. no address **A study of therapeutic innovation.** Cambridge, MA, M.I.T. Press, 1974. 340 p. L8.75.

The history of the use of chlorpromazine in psychiatry is surveyed. The synthesis and early clinical trials of chlorpromazine are reviewed, and the subsequent large-scale adoption of the drug for the treatment of a variety of psychiatric disorders is analyzed. Questions are posed regarding the effectiveness of chlorpromazine and its sister drugs, and the impact of these drugs on shifting the burden of psychiatric care from the State to public welfare and social agencies is considered.

225055 Rollin, Henry R. no address **The misuse of drugs in the treatment of the chronic psychoses.** World Medicine (London). 10(16):55, 57, 59-60, 1975

To determine if the use of psychotropic drugs in chronic psychotics is necessary, all medication was withdrawn from a group of 53 hospitalized patients (46 of whom were schizophrenics) for an initial one year period. The only complaint after withdrawal was sleeplessness in eight patients who had become drug dependent. In five of the eight, night medication with a placebo relieved sleeplessness. In the case of patients receiving psychotropic drugs, side-effects subsided. The eruption of symptoms in some patients was attributed to the natural history of the mental illness. A 7 year followup of 11 of the original patients suggests that withdrawal of drugs was not detrimental and in some cases was beneficial.

225152 Cooper, J. R.; Bloom, F. E.; Roth, R. H. no address **The biochemical basis of neuropharmacology.** London, Oxford University Press, 1974. 272 p. L2.50

An introduction to the basic concepts of central nervous system (CNS) biochemistry, physiology, and neuropharmacology is presented. After a review of the structure and functions of brain cells, CNS chemistry is discussed, with emphasis on the biochemistry of synapses. The implications of neuropharmacological findings for behavioral issues are discussed, and a chapter is devoted to memory mechanisms.

225158 Carlton, Peter L. Dept. of Psychiatry, CMDNJ, Rutgers Medical School, Piscataway, NJ 08854 **On neurochemistry and behavior.** Federation Proceedings. 34(9):1793-1795, 1975.

Historical antecedents to the development of behavioral pharmacology as a discipline are discussed. Roots of the new specialty are traced to the introduction of chlorpromazine and reserpine in psychiatric practice. The behavior that brought behavioral pharmacology to the forefront was that seen in conditioned avoidance situations. The goal of behavioral pharmacology is the characterization of drug action in the intact animal. As a discipline, behavioral pharmacology is characterized by an empirical stress on behavioral phenomena and by a behavioral language which has been stripped of excess meaning or "loaded" terminology.

225399 Forrest, Irene S.; Carr, Jelleff C.; Usdin, Earl. no address **Phenothiazines and structurally related drugs. Advances in biochemical psychopharmacology.** New York, Raven Press, 1974. 804 p. Vol. 9, $35.00.

The proceedings of the Third International Symposium on Phenothiozines and Related Compounds held in 1973 are summarized. In addition to the phenothiazines, related compounds such as the thioxanthenes are discussed in a series of sections similar to the sessions at the symposium. The material is addressed to clinical psychopharmacologists and psychiatrists concerned with the research aspects of antipsychotics.

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